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CONTROL OF THYREOTOXICOSIS BY METHYL THIOURACIL.[1]

By HUGH R. G. POATE,
Sydney.

SINCE the report in THE MEDICAL JOURNAL OF AUSTRALIA of April 13, 1946, by S. Livingstone Spencer and myself,[1] detailing the results of long-continued treatment by thiourea in our earlier cases and then by thiouracil in 75 patients with thyreotoxicosis, a further 25 patients in whom treatment had been concluded for a minimum period of six months were mentioned in an article by me published in THE MEDICAL JOURNAL OF AUSTRALIA, December 7, 1946.[2][3]

The original series had been checked up to the end of February, 1946, and the further 25 cases at the end of August, 1946, but all patients have been requested to report any recurrence. Of these 100 cases a satisfactory clinical result was obtained in 84; since then a further twenty patients have been treated with thiouracil, all but one with good clinical results and without any toxic reactions. In September, 1945, a supply of methyl thiouracil was made available and treatment of a new series of patients with this compound was entered on; and, as this drug later was placed on the market, all patients are now treated with it.

Material.

On September 11, 1946, I reported the results of the treatment of 38 patients with methyl thiouracil,[3] checked to the end of August, 1946, in an address at a State meeting of the Royal Australasian College of Surgeons in Adelaide, and the salient portion of this address was published in THE MEDICAL JOURNAL OF AUSTRALIA, December 7, 1946. In a criticism of these results Ivan Maxwell, of Melbourne, in a letter published in THE MEDICAL JOURNAL OF AUSTRALIA, January 11, 1947, page 62, drew erroneous conclusions from his consideration of seventeen "Reports of Cases" listed by us as examples of difficulties and unusual reactions. He failed to correlate these cases with the context of the article as we pointed out in our letter published on February 22, 1947. He made the following remarks:

> Now these are cases from the groups which Mr. Poate states are amenable to "thio" treatment. It is logical to assume that if Mr. Poate has so overstated the therapeutic value of "thio" drugs in this paper, it is probable that his present report which is unsupported by illustrative cases is equally misleading. This is particularly undesirable when thiouracil is available to all practitioners and so may be used indiscriminately.

In order that there can be no misapprehension as to results or the conclusions one has drawn, a summary of the histories of 84 patients treated with methyl thiouracil is appended. Since September 1, 1946, a further 25 patients have completed treatment, and along with the original series of 38 treated with methyl thiouracil form the basis of this present survey. These cases have been checked to March 31, 1947. A total of fifty patients with acute primary thyreotoxicosis is now presented along with six suffering from adenomatous goitre and seven with thyreotoxicosis recurring after deep X-ray therapy or operation. One case of recurrence in the thiouracil series has taken place and one in the methyl thiouracil series, both of which will be referred to later.

General Consideration.

It may be mentioned at this stage that all my patients are from private practice and have been referred by their own doctors. When practicable many patients are treated by their own medical attendants under my direction and I see them at intervals of about six weeks. In a few cases once the stage of "adequate response" has been reached, patients from the country have been allowed to return home under the care of their own doctor. I wish to

[1] Read at the State meeting of the Royal Australasian College of Surgeons, Perth, Western Australia, on April 21, 1947.

acknowledge the excellent liaison that has existed between the various country and suburban doctors and myself as they have been most meticulous in forwarding detailed reports. Except in large centres, such as Newcastle and Orange, it is not possible to have estimations of the basal metabolic rate carried out, but in most instances leucocyte counts have been done regularly and in none of these cases has there been any untoward happening.

A number of patients with toxic adenomatous goitre have been prepared for operation with either thiouracil or methyl thiouracil and then with iodine for two to three weeks prior to operation. None of these cases are included as they were all of short term treatment and the patients were submitted to operation.

In no case has carcinoma of the thyreoid with thyreotoxicosis been treated with "thio" compounds as the patients are referred at once for deep X-ray therapy. As previously pointed out, it would be unwise to use "thio" compounds in such cases as experimentally it has been shown that thiouracil renders the thyreoid gland more sensitive to carcinogenic substances.

Included in this report are nine patients with adenomatous thyreoids treated on an average for eight months; two of them finally agreed to operation, but the other seven either refused operation or were considered bad surgical risks. Also included are ten patients suffering from recurrent thyreotoxicosis after previous deep X-ray therapy or operation, six of whom have had excellent results with methyl thiouracil. Details are also given of twenty-one patients who are still continuing treatment, but who have reached the stage of "adequate response" and are on maintenance dosage. The grand total of cases under consideration is thus eighty-four and the various conclusions arrived at are based either on this series as a whole or on the fifty cases of acute primary thyreotoxicosis, in which treatment has been concluded.

Table I shows the patients grouped into the classes as mentioned in previous articles. There were nine males and seventy-five females. In this series, seven patients were subjected to operation and one was referred for deep X-ray therapy, and they are all included in the total of sixty-three whose treatment had been completed. In the remaining fifty-five cases the clinical results were very good as far as the control of thyreotoxicosis was concerned, that is, 87%, but in several instances there was still some prominence of the eyes and obvious thyreoid enlargement. In those cases in which some exophthalmos and thyreoid hyperplasia of less than six months' duration were present, a return to apparent normal was effected by the use of *Thyroideum Siccum* as soon as zero or *minus* metabolism was reached and carried on during the period of maintenance dosage. As experience has been gained the use of *Thyroideum Siccum* has been instituted earlier and continued for a longer period, often up to six months, but as a rule its maximal effect is obtained in about three months. As soon as this form of therapy is instituted, a close watch must be kept on the pulse rate and the basal metabolic rate, as it may tend to rise and a larger maintenance dose of methyl thiouracil must be used. (See Case 44, Class II.) It is seldom that symptoms of myxœdema are induced if regular estimations of basal metabolism are made and the patient is kept under regular observation (Case 72, Class I, is an example), but this is quickly controlled by the use of *Thyroideum Siccum* for a few weeks and reduction of the dose of methyl thiouracil.

The principles of treatment and dosage were discussed in the article published on December 7, 1946, and further experience confirms the views then expressed, but mention must again be made of the necessity for maintaining a zero or *minus* metabolism for a minimum of three months and preferably for four months before treatment can be suspended without risk of relapse. If treatment is suspended as soon as a normal metabolism has been restored, relapse is apt to occur within six to eight weeks and many such cases are referred to in current literature showing that this principle has not been appreciated. It will be noted that in many cases treatment is commenced at once so as to save the week or two before the basal metabolic rate can be determined, but a leucocyte count is done at once.

Results.

The term "adequate response" is used to denote a reduction in the basal metabolic rate to a zero or *minus* figure. It will be seen in Table I that the average time for all cases in which no iodine has been exhibited prior to treatment with methyl thiouracil is five and a half weeks, whereas with those in which iodine has been given it is over ten weeks, although in groups I and III there is a much wider discrepancy. Despite this slow response, there is not a corresponding difference in the average time of treatment, there being only a month longer in the iodine cases, but the greatest difference is seen in patients under twenty-five years of age. It is advisable therefore when seeing a thyreotoxic patient for the first time not to give any treatment other than sedation and adjuvant dietary therapy until such time as it can be determined whether the patient will be given a trial on methyl thiouracil or is to be referred for operation. In the latter event it is unwise to give iodine until a week or two prior to the patient's admission to hospital.

In the fifty cases of acute primary thyreotoxicosis in Classes I, II and III, 41 patients had the usual evenly enlarged hyperplastic gland frequently associated with some degree of lid retraction or mild exophthalmos and were treated with *Thyroideum Siccum* as soon as the metabolism came to zero, with return to normal in 28 cases. In the other 13 patients who had a relatively long history, improvement was noticed as regards the eyes in most instances, but the thyreoid remained enlarged. Five patients were operated upon, two being reported previously (*Cases 27, Class IV, and 28, Class II*) (*December 7, 1946*). One young woman (Case 47, Class II) had a febrile

TABLE I.
Patients with Thyreotoxicosis Treated with Methyl Thiouracil.

Class.	Numbers.		Treatment Concluded.	Treatment Continuing.	Average Time for Treatment. (Months.)		Average Time for Adequate Response. (Weeks.)		Operated On.
	Male.	Female.			No Iodine.	With Iodine.	No Iodine.	With Iodine.	
Under 25 years	0	6	5	1	5½	9	4	10	—
25 to 45 years	3	38	32	9	6½	7½	6½	9½	3
Over 45 years	3	15	13	5	6½	7½	5½	14	1
Toxic adenomata	0	9	6	3	8	—	7	—	3
Recurrent after X ray or operation	3	7	7[1]	3	6	6	5	8½	—
	9	75	63	21	6½	7½	5½	10½	7

[1] One patient referred back for further deep X-ray therapy.

reaction and desired operation. Two others had responded satisfactorily, but one (Case 50, Class II) wished operation for cosmetic reasons, and in the other (Case 51, Class III) an adenoma of the right lobe of the thyreoid became evident, when after five months' treatment the general hyperplasia had cleared. One patient (Case 38, Class V) who had been operated on in 1939 and had two courses of deep X-ray therapy in 1943, could not tolerate the drug and was referred for further deep X-ray therapy.

Taking the 63 cases in which long-period treatment with methyl thiouracil had been completed or attempted and abandoned because of toxic reactions, we find that one patient was referred back for deep X-ray therapy (Case 38, Class V), two were operated on after febrile reactions (Cases 27, Class IV, and 47, Class II), two were operated on for cosmetic reasons after a good response (Cases 28, Class II, and 50, Class II), one was operated on who responded well but relapsed and was subsequently found to have an adenoma (Case 51, Class III), and two with multiple adenomata were operated on who responded well for the first two months but in whom toxicity recurred during early maintenance therapy (Cases 56 and 67, both Class IV) as is so common with toxic adenomata. In Cases 28 and 50 (both Class II) response to the drug had been very good and they should not be classed as failures. If this point is allowed, it means that in 57 of the 63 cases under discussion, that is, in 90%, control of the thyreotoxicosis persisted for at least two months and up to fifteen months after cessation of treatment by methyl thiouracil. If all the cases in which operation was performed are regarded as failures the percentage of apparently good results is 87. I must admit that these results have been a surprise and the patients and figures have been checked and rechecked, so I do not think there is any doubt as to their accuracy. As a surgeon I undertook the trial of these "thio" drugs with some scepticism, but it was soon proven that they were most efficacious as a pre-operative measure and then the trial was begun of using them as a possible curative measure. The results now presented speak for themselves without any expression of optimism or enthusiasm from me, but I can say definitely that thyreoid surgery today is a very different matter to what it was even two or three years ago, largely owing to the advent of the "thio" drugs.

Toxic Effects.

In Case 14 (Class II) the patient had mild cervical adenopathy, and in Case 16 (Class II) the patient had a mild febrile reaction for which treatment was stopped for twenty-four hours. In Case 27 (Class IV) the patient was the woman who had some febrile reaction and later developed recurrence of an exfoliative dermatitis—this case is being reported fully in the *Proceedings of the Royal Australasian College of Physicians* (July, 1946, Volume I, Number 2). These cases were reported in the article of December 7, 1946. In Case 38 (Class IV) the patient had an initial leucocyte count of only 3,900 per cubic millimetre and developed a leucopenia of 2,500, but she had 54% granulocytes. She also developed an ulcerated mouth. She was referred for further deep X-ray therapy. In Case 40 (Class V) the patient had slight erythema on the arms, but treatment was not stopped. In Case 41 (Class I) the patient had a very mild febrile reaction of 99° F. Her physician stopped treatment, but renewal was advised a week later. In Case 45 (Class IV) the patient had slight erythema on the arms with a sore throat, but treatment was not stopped as this occurred in the eighth week of treatment and was thought not to be due to the drug. In Case 47 (Class II) the patient had a severe febrile reaction after a mild reaction a week previously; she was operated on after iodine preparation. In Case 57 (Class III) the patient complained of diplopia in the sixth month of treatment. She had paresis of the left inferior oblique muscle for no apparent reason; it cleared two months later. In Case 64 (Class II) the patient had been mentally unstable for some months prior to the institution of treatment. She had been taking thyreoid substance to reduce weight for several months. She became psychotic after four months' treatment, although physically well.

When these cases are reviewed it is doubtful whether the drug was the ætiological factor in Cases 38, 40, 45 or 64, but as these troubles developed during treatment they are mentioned. This list of toxic reactions is relatively small.

The Leucocytes.

In 56 of the 84 cases listed there was an increase in the number of leucocytes during treatment, but the number tended to return close to the original count during the maintenance period of dosage. In the remaining 28 cases there was a fall of one or two thousand, but except in Case 38 (Class V) there did not seem to be any cause for worry. In this instance the patient had an initial count of 3,900 per cubic millimetre with 58% neutrophile cells, and the number fell to 2,500 with 51% neutrophile and 3% eosinophile cells. Although the percentage of neutrophile cells rose to 77% later, the total count did not exceed 4,000 per cubic millimetre. In Cases 44 (Class II), 56 (Class IV) and 75 (Class V) there were initial counts below 4,000 per cubic millimetre, but they all rose to normal levels during treatment. Four other patients are worthy of note as having a relatively low neutrophile percentage—Case 19 (Class V), a total of 5,900 per cubic millimetre with neutrophile cells 39%; Case 47 (Class II), a total of 10,900 per cubic millimetre with neutrophile cells 35%; Case 55 (Class II), a total of 5,000 per cubic millimetre with neutrophile cells 24%; and Case 77 (Class I), a total of 5,500 per cubic millimetre with neutrophile cells 40%. In all these cases a close watch was kept on the white cells, but nothing abnormal developed. One fairly constant feature was the increase in eosinophile cells usually to about 3%, but in 29 cases they went up as high as 14%, except in Case 27 (Class IV) which compels special mention. It was thought that an unusual eosinophile count might indicate a toxic reaction. This does not appear to be the case except when there is an initial eosinophilia of 10% or more indicative of an allergic state and these patients require careful watching.

In Case 27, a woman of fifty-one years had two years previously a severe nasal hæmorrhage necessitating blood transfusion which was followed by a severe exfoliative dermatitis. It was noticed then that she had thyreotoxicosis for which iodine was given. Two weeks before being seen she had another severe nasal hæmorrhage. She had a large adenomatous thyreoid, a pulse rate of 140 or so with auricular fibrillation and was a very sick woman. The blood findings are shown in Table II.

TABLE II.

Date.	Red Cells per Cubic Millimetre.	Hæmoglobin.		Leucocytes per Cubic Millimetre.	Neutrophile Cells *per Centum.*	Lymphocytes *per Centum.*	Monocytes *per Centum.*	Eosinophile Cells *per Centum.*
		Grammes.	*Per Centum.*					
8.3.46	3,480,000	7·2	42	5,000	66	25	8	11
26.3.46	3,900,000	9·3	54	8,000	50	28	4	18
30.3.46	Transfusion 1 litre blood.							
2.4.46	4,400,000	13·8	80	8,000	52	22	2	24
24.4.46	—	—	—	6,200	49	24	8	19

XUM

On March 3, 1946, methyl thiouracil 0·1 gramme was given every eight hours. On March 15 a slight erythema was noticed on exposed areas, so bromide was suspended. From March 18 to 23 an irregular but gradually rising temperature to 100° F. was noted, so all treatment was stopped. As the temperature fell to normal treatment was resumed three days later, 0·1 gramme being given every twelve hours, but this was suspended on March 28 as the temperature had risen to 100° F. and dermatitis became obvious. This subsequently went on to a generalized exfoliative condition. On April 27, 1946, a total thyreoidectomy was performed, and when seen four months later the patient was very well. The initial eosinophilia was overlooked, but it has since served as an object lesson.

General Remarks.

There were six cases with auricular fibrillation which disappeared in three to four weeks without any specific therapy in four cases, Cases 23 (Class III), 27 (Class IV), 75 (Class V) and 83 (Class III). In Cases 10 and 69 (Class V) both patients had a three-year history with fibrillation for eighteen and twelve months respectively, despite three courses of deep X-ray therapy, constant medical treatment and several visits to hospital. They both have still some irregularity in the pulse occasionally and take digoxin when they feel the need for it. In neither case was there any visible or palpable thyreoid gland and both patients are now well and leading active lives. With acute hyperplastic toxic goitre excellent results can be expected in 85% to 90% of cases, provided the principles of minimal dosage and adequate adjuvant therapy are followed. I have as yet failed to see a patient in this class resistant to "thio" therapy, but have seen several in my own practice and many in consultation with physicians who have failed to recognize an adenomatous goitre even after many months of continuous treatment. For example, a woman of forty-two years had been on 0·2 gramme of thiouracil for thirteen months with varying degrees of toxicity during this time; she had a large adenomatous thyreoid and did very well after total thyreoidectomy. The average gain in weight of those who had completed treatment was fourteen pounds, but considerable variation occurred from 0 to 42 pounds. In only one case was there a loss of three pounds.

The average time for the "adequate response" to a zero or *minus* metabolism in the 84 cases was eight weeks, but in those who had no previous iodine medication it was only a little over five weeks. As noted in the earlier series, this time was doubled in those who had been given iodine, although the average drop in the basal metabolic rate was very much the same, being 34% for those without iodine and 36% among those who had iodine.

In the latter half of the series *Thyroideum Siccum* was given in all cases in which there has been enlargement of the thyreoid gland, and it is now commenced at the first zero or *minus* metabolism, being continued until the eyes and the thyreoid are normal or discontinued after four months if this result is not achieved.

It is interesting to note that in some cases there is a prompt rise in metabolism, necessitating a smaller dose of *Thyroideum Siccum* or a larger dose of methyl thiouracil or perhaps both, so it is necessary to keep a close watch on progress for the first four to six weeks after this therapy is commenced. This reaction rather suggests that the control of thyroxin production is very finely balanced at the stage of "adequate response", and if treatment with "thio" compounds is stopped, then a recurrence of symptoms is apt to occur within a month or so. With a maintenance dosage sufficient to hold a zero metabolism for four months stability of a normal thyroxin production is obtained and the normal thyreotrophic hormonal balance between pituitary and thyreoid is also reestablished. It is in this stage that some additional thyroxin seems to be needed to establish this latter balance and so to overcome the thyreoid hyperplasia and the exophthalmos which appear to be governed by the thyreotrophic hormone. *Thyroideum Siccum* has been chosen as this is a standard British Pharmacopœia preparation containing 0·5 milligramme of thyroxin in a half-grain tablet and is available in smaller dosages as well. Only six of these 84 patients have been treated for a period of four to six weeks in hospital, and all the others have carried on with their usual duties except the referee of wrestling who was persuaded to give up this activity for two months. This method of ambulatory treatment is of great economic importance to patients, and in no case has there been any complaint as to the time given to the estimations of the basal metabolic rate, for leucocyte counts and for the necessary visits for follow up. It is usual to tell all patients that there is a chance of cure without surgery in four out of five cases and they are warned to cease treatment at once if any fever, rash or sore throat develops and to report immediately.

Adjuvant therapy in the form of regular mild sedation and a standardized preparation of mixed vitamin in adequate dosage for the individual is now a routine procedure. Supplementary vitamin *B* may be advisable, and if there has been any undue loss of weight a diet with a high protein content is given. The only articles of diet forbidden are members of the Brassica family, for example, cabbage, cauliflower, brussel sprouts and broccoli, because of the cyanogen content, which is apt to induce or to increase hyperplasia in the thyreoid. It was hoped that propyl thiouracil would prove more efficacious than other preparations, but in a personal communication from London advice has been given that clinical trials were unsatisfactory and its manufacture for general use has been abandoned. Reports from America had been rather favourable, but the results had not been confirmed in England.

However, McGavack and co-workers[18] have just reported 75 patients treated with propyl thiouracil with only one instance of toxic effect in a woman who developed a rash and fever, but who had been proven sensitive to thiouracil previously. In ten cases treatment had been suspended for at least four months without any recurrence. McGavack and his collaborators consider it far superior to thiouracil and a safe and effective drug for the management of all forms of hyperthyreoidism. Astwood and Vander Laan[17] had reported favourably on propyl thiouracil in December, 1945, and considered it had no apparent side effects.

Thiobarbital has been discarded, as it induced too many toxic reactions (Astwood).[4]

Abstracts from Current Literature.

In discussing remissions in thyreotoxicosis after discontinuing thiouracil, Bierwalter and Sturgis[5] draw attention to the importance of differentiating between nodular and non-nodular toxic goitres. They point out that in the former the response to thiouracil is less satisfactory, the symptoms are insidious in onset, there is less tendency to natural remissions in the course of the disease and a certain number of goitres become carcinomatous. They draw attention to three findings: (i) recurrence occurs almost always within two months if the drug is given for a short period—usually less than six months; (ii) if remission of symptoms persists for more than two months after thiouracil is discontinued, the tendency is for it to continue; (iii) of patients treated adequately for more than six months 80% have a remission of symptoms lasting longer than the critical two months. They advise operation in all cases of nodular goitre. Of the 80 patients whom they discuss 45 had non-nodular goitre, and of the latter four were operated on because of toxic reactions or at the request of the patient. In eight cases in which the average length of treatment was 10·6 months the patients were well six months after ceasing treatment. Five cases recurred promptly when treatment was interrupted after three and a half months. They conclude as follows: "In the treatment of selected cases of thyreotoxicosis, therefore, thiouracil treatment must be considered as a form of therapy which has promise and ultimately it may prove to be as satisfactory as thyroidectomy in this group of patients."

The same authors,[6] in discussing contributing factors in fatal agranulocytosis, consider that the following points, if kept in mind, will avert, or reduce to a minimum, fatal reaction in agranulocytosis: (i) Penicillin in adequate doses must be administered promptly. (ii) Discontinuance of the drug must be immediate upon onset of symptoms. (iii) Any significant symptoms suggesting the onset of the condition must never be disregarded. (iv) The usually

accepted forms of therapy for the condition are inefficient. (v) If leucopenia develops the drug must be discontinued.

Other authors find repeated small blood transfusions helpful, also administration of pyridoxine, vitamin *C* and folic acid, this last mentioned being the active substance in liver which exercises the protective effect on the granulocytes. Astwood in June, 1944,[8] reported on eighteen patients treated with thiouracil. In nine of them who had only short-period treatment recurrence was prompt, but in the case of the other nine treated for six and a half to eight months results were good from two to nine months later.

Barr and Schorr[9] reported 61 patients completing treatment with thiouracil. In 13 cases the period of treatment was less than six months and four patients relapsed. In 48 treated for longer than six months, 11 relapsed, and six of them within one month of ceasing treatment. In all 77% of patients did not relapse after six months in half the cases and less than two months in the other half. Among the 100 cases discussed there were two cases of agranulocytosis and in two others leucopenia led to treatment being abandoned.

Edson Fowler[10] in a collective review from 69 clinics remarks:

> It will be of great value to know in what type of patient a permanent cure can be anticipated, particularly since, if a cure is expected, many patients would prefer even prolonged medical management with thiouracil to surgery. It seems obvious that unless the incidence of toxic reactions to thiouracil is low and the incidence of permanent cure is high, thiouracil therapy is therapeutically and economically unsound except in those patients who are poor operative risks following iodine therapy or who refuse surgical treatment.

However, he leaves the question unanswered.

R. H. Williams[11] reports 247 patients treated with thiouracil of whom 121 or 49% were subjected to operation. Of the total number 29% had nodular goitres, 14% had previous thyreoidectomy and 34% had been treated with iodine. Iodide was given during part or all of the period of thiouracil therapy in 29% of cases, and in these most of the patients were subjected to thyreoidectomy. In 9% of cases thiouracil was replaced by iodide for various reasons. Of 100 patients treated with thiouracil 49 have gone for intervals of three to twenty-one months free of symptoms. In 51 cases there was relapse within one month of the cessation of treatment, and among these ten patients had nodular goitre. Patients treated for nine months or longer showed a better sustained response than those treated for shorter periods.

Of the 121 patients operated upon it is stated that in the majority of cases in which treatment with iodine was used, this drug was given during the last few weeks of thiouracil therapy.

In considering the question, "What, now, is considered the place of thiouracil in the treatment of thyreotoxicosis either with or without thyreoidectomy?", Williams remarks that only tentative conclusions can be drawn as further experience with thiouracil and other antithyreoid compounds may well change present impressions.

A. Wilson, of Sheffield, reports forty patients treated with thiouracil and thirty with methyl thiouracil and favours the latter drug. Among the seventy patients were five with anxiety neurosis who were not benefited. Nine patients were operated on, five having adenomatous toxic goitre and four hyperplasia. In fifty-six cases control of thyreotoxicosis was maintained satisfactorily whilst the patient was on treatment. In eighteen cases therapy was withdrawn, in twelve before and in six after a satisfactory maintenance had been determined, but fifteen patients relapsed. Wilson concludes: "The evidence is strongly in favour of continuing administration of thiouracil in small maintenance doses without interruption."

Himsworth, Morgan and Trotter[12] compared end results in 93 cases of toxic goitre in which the patients were subjected to thyreoidectomy with 91 patients treated with thiouracil; but if we can judge from our own standards there were too many complications on either side and a mortality rate of 2% in both cases was unduly high. From the point of view of permanent remission in thyreotoxicosis 25 patients were reported as showing a good response, but seven relapsed in periods varying from six to thirty months. In all cases the patients who relapsed had been treated for less than twelve months and the average basal metabolic rate on the conclusion of treatment was over +10%, a figure which we regard as evidence of persisting toxicity.

In a leading article in *The Lancet*[14] discussing these results it is stated that "treatment cannot be discontinued as soon as symptoms are under control, it must be continued for a long time". Also the following significant comment is made which supports our insistence on a three to four months period of maintenance of a *minus* metabolic rate before treatment is discontinued: "It is perhaps a matter of controlling thyreoid secretion until the abnormal pituitary stimulus, or some other disturbance a stage beyond that, has died away, or possibly until the thyroid itself has become relatively unresponsive to higher stimuli."

Rose and McConnell[15] analysed 35 cases they had on prolonged treatment with thiouracil and divide them into three groups: (i) Remission occurred up to eleven months following cessation of treatment in sixteen cases of which fifteen were the diffuse type of goitre. There were four relapses when the drug had been withdrawn too soon. (ii) Patients remaining in remission on small doses numbered thirteen with eleven relapses readily controlled. Therapy had been continued six to twenty months. (iii) Six cases were classed as unsatisfactory after seven to twenty-six months' therapy; three were cases of nodular goitre, but four patients had complicating diseases, for example, diabetes, hypertension *et cetera*. Rose and McConnell conclude that the best results are obtained with the moderately toxic diffuse types. They consider that there is not a sufficiently high percentage of remissions (45·7%) to compare favourably with operative results.

Elmer Bartels,[17] discussing the possibility of thiouracil as a curative agent in thyreotoxicosis, quotes 21 cases of his own in which treatment had been suspended, but thirteen patients relapsed mainly within six months; in ten of these treatment had been carried on for very short periods of one to four months, whereas in the eight cases of remission five patients had been treated for seven to twenty-one months. He gives figures from nine other clinics totalling with his own cases 274, which show 51·5% of patients with remissions and 48·5% with relapse after discontinuing treatment with thiouracil. There were five clinics which had less than twenty cases each, and Williams *et alii* topped the list with 100 cases to which reference has already been made. Six other reports have been found totalling 139 cases with 54·6% of remissions and 45·4% of relapse.

Our own figures for thiouracil and methyl thiouracil now total 183 patients who have concluded therapy with 24 who had unsatisfactory results; most of the 24 patients have been operated on, and this leaves 159, of whom to date only two have relapsed, that is, 1·2%. There is such a tremendous discrepancy in the figures that one is compelled to ask: "Why?" The answer seems to be in our method of dosage, which varies for each individual according to the response, the maintenance of a *minus* metabolism for three to four months before discontinuance of therapy, the exclusion of all patients with nodular toxic goitres who can be brought to operation, and the importance given to adjuvant therapy and diet right through the whole period of treatment.

Geo. Crile, junior, and R. S. Dinsmore[16] in an excellent review of the present status of the surgical treatment of hyperthyreoidism state that "the surgical treatment of diffuse goitre with hyperthyroidism is empiric in approach, unpredictable in outcome and unphysiologic in principle, but from a clinical standpoint is safe, simple and satisfactory". They consider that thiouracil accomplishes a physiological instead of an anatomical thyreoidectomy. "If thiouracil were less toxic and large doses could be given safely over a long period of time to produce a true myxœdema and to maintain it for several months the 'vicious circle' might be so completely interrupted that

TABLE III.

Class I. Under 25 Years. Six Cases.

Case Number; Age (Years); Date Seen; Length of History.	Date.	Basal Metabolic Rate.	Weight in Pounds.	Pulse Rate per Minute.	Leucocytes per Cubic Millimetre.	Percentage of Neutrophile Cells.	Result.	Remarks.
15 Mrs. H.C.M. 23 years 11.3.46 3 months.	11. 3.46 2. 4.46 12. 6.46 11. 7.46 8. 8.46	+26% −2% −27% −12% −1%	118 123 130 132 134	124 80 80 84 80	8,800 7,400 7,000 8,100 9,600	45 58 52 54 53	Excellent.	Typical acute Graves's disease—lost 21 lb. weight. Treated by her own doctor under direction. Pregnant in July, 1946. Seen 1.10.46. Pulse 80, weight 139 lb. Seems normal.
30 Miss G.M. 15 years 8.2.46 2 years.	8. 2.46 30. 4.46 5.12.46	+16% +2% +9%	105 106 111	108 84 96	— 5,800 8,000	— 68 72	Excellent.	Had been treated with iodine for 2 years. Thyreoid enlarged. Eyes prominent. Treated by her doctor in country under direction. Seen 17.3.47. Clinically normal.
41 Nurse B. 22 years 20.10.46 1 month.	13.11.46 30.11.46 8.1.47 19. 2.47	+15% +5% −12% +6%	— — — —	110 92 74 78	5,900 6,200 5,200 6,000	62 67 57 60	Excellent.	Was given thiouracil 2 weeks previously but ceased because of temperature 99° F. Recommended 3.11.46. Note that first B.M.R. was determined 13.11.46. Returned to theatre duty —.12.46. 30.3.47 apparently normal.
48 Miss M.F. 15 years 13.9.46 9 months.	23. 8.46 1.10.46 16.10.46 29.10.46 12.11.46 16.12.46 21. 2.47	+43% +27% −1% −12% −5% −19% −2%	128 130 134 138 143 151 150	132 136 100 96 90 80 100	10,200 5,800 9,000 7,300 7,400 5,800 —	75 45 48 58 40 46 —	Excellent.	Had been on iodine for 3 months. 8.11.46 started on *Thyroideum Siccum* gr. ½ b.d. as eyes were prominent and thyreoid enlarged. 20.3.47, treatment ceased a month ago and is clinically normal.
72 Miss J.L. 23 years 5.3.46 6 months.	15. 3.46 8. 4.46 30. 4.46 31. 5.46 5. 7.46 5. 8.46 13. 1.47	+19% −5% −8% −17% −10% −27% −29%	144 147 149 145 148 149 152	126 — — 84 — — 72	— — Reported as	— — normal.	Excellent.	A nurse at a suburban hospital treated by her doctor under direction. Remained on duty. 13.1.47, given *Thyroideum Siccum* because of low B.M.R. 14.2.47, clinically normal.
77 Mrs. H.M.R. 24 years 14.12.46 6 months.	18.12.46 9. 1.47 23.1.47 20. 2.47	+22% −8% −20% −11%	105 112 113 116	140 86 68 78	5,500 10,300 9,300 8,000	40 53 51 50	Continuing.	Baby 9 months old. 24.1.47, was given *Thyroideum Siccum* gr. ½ b.d. as thyreoid was enlarged and eyes prominent. 30.3.47, condition appears normal. Final result should be excellent.

Class II. 25 to 45 Years. 41 Cases.

2 Mrs. L.B. 32 years 11.3.46 6 months.	11. 3.46 22. 8.46	+34% −1%	121 127	120 72	5,400 8,800	69 60	Very good.	Treated in country under direction. After 6 weeks pulse 80, weight 127 lb. and felt very well. Amenorrhœa of 18 months' duration ceased 6.4.46. 7.5.46, *Thyroideum Siccum* advised as thyreoid was still enlarged. Final result very good.
3 Mrs. O.M.D. 26 years 28.12.45 3 months.	20.12.45 21. 2.46 21. 3.46 13. 6.46 18. 7.46	+28% +9% −1% −8% −6%	122 115 114 115 119	96 84 68 66 70	8,800 6,200 12,400 8,000 —	58 70 68 — —	Excellent.	18.7.46, clinical result excellent and stated she had not felt so well for years.
4 Mrs. T.M.F. 33 years 7.3.46 9 months.	7. 3.46 30. 3.46 24. 4.46 20. 5.46 15. 7.46 30. 8.46 1.11.46 21. 2.47 25. 3.47	+33% +23% +10% −1% +10% +6% −2% +13% +8%	108 112 115 113 114 112 110 103 101	120 96 84 80 90 84 80 100 84	5,700 6,000 6,400 9,600 5,200 4,600 5,600 5,300 8,700	53 67 76 74 48 54 53 62 71	Fair.	Treated with iodine for some months and thyreoid enlarged steadily. 3.6.46, *Thyroideum Siccum* gr. ½ b.d. ceased 16.7.46 as eyes normal, but thyreoid still enlarged and B.M.R. had risen. Clinically, condition satisfactory. Had a lot of family worries and overwork, January-February, 1947. Home conditions unsatisfactory.
5 Miss M.F. 30 years 3.12.46 1 year.	23.11.45 19. 2.46 16. 4.46	+46% ±0% +2%	105 119 121	140 80 76	8,600 7,500 8,200	55 61 78	Very good.	31.1.46, *Thyroideum Siccum* gr. ½ b.d., as thyreoid had enlarged. 3.8.46, condition very good, but thyreoid enlarged.
6 Mrs. M.F-sn. 33 years 12.12.45 2 years.	7. 9.45 17.11.45 29. 1.46 27. 3.46 29. 5.46	+41% +36% +15% ±0% ±0%	— 98 — 110 111	— 120 78 76 70	Reported as	normal.	Excellent.	Was treated with iodine on several occasions. Treated under direction by her own doctor. Thyreoid was enlarged but subsided with *Thyroideum Siccum*. January, 1947, clinically normal.
8 Mrs. I.H. 39 years 7.11.45 1 year.	30.10.45 6.12.45 21.12.45 7. 2.46 5. 3.46	+26% +14% −8% −16% —	125 127 129 138 142	106 88 80 70 70	8,000 5,200 6,000 7,200 —	59 60 64 45 —	Excellent.	Urticaria for 14 months. Mental state unbalanced. Amenorrhœa since 28 years of age. 21.12.45, *Thyroideum Siccum* as thyreoid and eyes involved. 28.9.46, apparently normal mentally and physically.
12 Mrs. L.M.K. 34 years 28.12.45 2 years.	28.12.45 10. 1.46 6. 2.46 13. 3.46 8. 4.46 13. 5.46	— +13% +3% +10% −24% −8%	111 118 118 119 121 122	120 100 80 66 70 70	6,400 — 7,400 5,700 5,000 5,300	49 — 75 62 71 60	Excellent.	Thyreoid enlargement after childbirth 6 years ago cleared with iodine. Recurred after second child 2 years ago, but no reaction to iodine and developed typical Graves's disease. Amenorrhœa. Given *Thyroideum Siccum* 28.2.46. 9.7.46, apparently normal in all respects.

TABLE III.—*Continued.*

Class II.—Continued.

Case Number; Age (Years); Date Seen; Length of History.	Date.	Basal Metabolic Rate.	Weight in Pounds.	Pulse Rate per Minute.	Leucocytes per Cubic Millimetre.	Percentage of Neutrophile Cells.	Result.	Remarks.
13 Mrs. S.McL. 37 years 28.2.46 3 years.	6. 3.46 20. 3.46 30. 3.46 1. 5.46 31. 5.46 28. 8.46	+46% +24% +2% ±0% +7% +6%	98 106 105 102 99 98	120 84 78 80 84 74	13,200 5,600 8,600 7,600 — 7,700	67 47 72 57 — 65	Excellent, but relapsed.	Eyes prominent. Thyreoid enlarged. 8.4.46, *Thyroideum Siccum* gr. ½ b.d. 29.11.46, apparently normal. February, 1947, condition relapsed. See special report.
14 Mr. H.M. 32 years 12.2.46 3 months.	17. 1.46 26. 2.46 11. 3.46 26. 3.46 15. 4.46 23. 4.46 7. 5.46 21. 5.46 20. 6.46 17. 9.46	+21% +11% ±0% +10% +20% +11% +3% −2% +5% −3%	122 121 126 131 133 132 132 131 133 141	110 100 80 74 70 74 76 74 78 72	— 4,800 5,100 5,200 9,300 8,600 8,000 6,400 9,000 —	— 53 66 71 62 66 60 64 65 —	Excellent.	No thyreoid palpable, but became so during treatment. Had slight cervical adenopathy. He did not keep to regular treatment in March and April, 1946. Mental state was peculiar, but later became normal and he was then most cooperative. Final result excellent but eyes slightly prominent.
16 Mrs. L.V.M. 29 years 6.1.46 8 months.	1.11.45 5. 1.46 22. 1.46 5. 2.46 12. 3.46 28. 6.46	+54% +23% −1% +10% +5% +7%	129 136 — — 135 147	120 100 120 100 100 100	8,200 8,000 — 7,700 9,200 7,100	74 77 — 66 61 70	Excellent.	A very acute case and was at rest with sedation pending going to hospital after Christmas. On fourth day temperature 99·6° F. Treatment stopped for 2 days. 13.12.46, weight 145 lb., pulse 80. Apparently normal.
20 Mrs. F.C.R. 40 years 11.3.46 7 months.	3.12.45 16. 3.46 30. 4.46 10. 5.46 24. 6.46 6. 7.46 6. 9.46	+29% +16% ±0% −6% −3% −14% −6%	102 105 108 114 116 122 105	— 90 — 90 — 96 110	— 4,700 6,300 6,100 — — 5,700	— 62 66 55 — — 46	Excellent.	Had been under medical treatment 4 months. Was very anæmic. In August, 1946, had antritis; also gingivectomy. Final result excellent.
21 Miss N.E.R. 30 years 6.12.45 2 years.	6.12.45 8. 1.46 6.3.46 2. 7.46	+41% +6% −4% −17%	111 114 120 117	110 84 66 80	9,500 6,400 7,300 9,100	70 59 57 63	Excellent.	Large goitre, acute hyperplastic type. 25.3.46, given *Thyroideum Siccum*, which reduced the size of gland considerably. Seen 18.2.47. Condition normal except for an enlarged thyreoid.
24 Mrs. B.B. 26 years 22.1.46 3 months.	20. 1.46 5. 2.46 11. 2.46 26. 2.46 11. 3.46 30. 4.46 14. 6.46 11.12.46	+16% +19% ? −2% +3% −18% −6% −32% −3%	111 117 117 122 126 134 132 120	108 100 89 80 70 80 64 100	6,700 6,700 4,700 4,200 4,200 5,000 — —	58 60 58 70 45 54 — —	Excellent.	Was thought to be thyreotoxic in May, 1942, but B.M.R. −6%, and in October, 1943, −9%. Had a lot of worry and overwork on a farm—Husband overseas. Baby in October, 1945. 30.4.46, *Thyroideum Siccum* gr. ½ b.d. Seen 18.3.47; apparently normal. Weight 113 lb.
25 Mrs. D.R.H. 33 years 12.3.46 6 months.	7. 3.46 19. 3.46 2. 4.46 6. 8.46	+34% +5% −9% −30%	143 138 143 —	— — — —	4,900 6,000 4,000 —	38 34 57 —	Excellent.	Developed a few weeks after birth of third child. 2.4.46, *Thyroideum Siccum* gr. ½ b.d. The low neutrophile count was a feature.
28 Mrs. H.W. 32 years 17.2.46 6 weeks.	20. 2.46 14. 3.46 26. 3.46 10. 5.46 6. 6.46	+9% −12% +6% −15% −16%	72 — — 111 119	140 — — 100 110	6,200 — — 4,600 5,300	68 — — 61 61	Excellent. Operated upon.	Was a myasthenic type of acute thyreotoxicosis developing after a miscarriage, end December, 1945. Had a large goitre for many years, colloid type. 8.7.46, operation as was a secondary type. 7.8.46, condition splendid. Weight 123 lb.
29 Mrs. H.F. 38 years 14.12.45 2 months.	7.12.45 30. 1.46 27. 2.46 13. 3.46 2. 5.46 3. 6.46	+31% −5% +11% −4% −7% −2%	127 140 142 142 142 143	130 100 86 80 80 76	8,000 5,900 9,200 10,000 7,900 9,400	53 62 58 61 62 66	Excellent.	7.2.46, *Thyroideum Siccum* gr. ½ b.d. Note elevation of B.M.R. 27.2.46, had prominent eyes and very large thyreoid swelling, which was barely noticeable on concluding treatment.
33 Mrs. S.McL. ? years 11.3.46 4 months.	11. 3.46 30. 4.46 5. 7.46 1. 8.46	+28% +1% −2% +11%	114 125 132 140	110 88 96 86	6,600 4,800 6,000 6,200	58 57 62 63	Fair. Continuing.	Had a colloid goitre since a child. Toxicity has supervened only over last 4 months. Has aortic valvular incompetence. Clinical result satisfactory, but may require long-continued maintenance.
34 Mrs. M.R. 34 years 22.7.46 6 months.	30. 7.46 27. 8.46 11. 9.46 31.10.46	+13% +2% −3% −1%	156 158 156 161	100 92 80 80	6,500 5,950 4,500 7,300	49 75 54 72	Excellent.	Had enlarged hyperplastic gland. 24.9.46, *Thyroideum Siccum* given, but only slight subsidence of gland.
37 Mrs. V.G.T. 30 years 11.7.46 7 months.	27. 6.46 17. 7.46 1. 8.46 14. 8.46 28. 8.46 25. 9.46	+43% +41% +20% +2% −18% −6%	— 94 95 97 98 102	— 96 80 90 76 72	— 13,900 13,400 8,300 8,200 6,900	— 67 53 68 62 54	Excellent.	Large hyperplastic gland and prominent eyes. 11.10.46, *Thyroideum Siccum* gr. ½ b.d. 11.2.47, eyes normal; thyreoid noticeably less. General condition excellent.
39 Mrs. M.B. 33 years 20.8.46 18 months.	29. 8.46 12. 9.46 26. 9.46 10.10.46 7.11.46	+25% −8% +5% −9% −4%	118 126 130 134 137	92 92 68 72 72	5,800 10,800 8,000 7,300 6,900	67 60 60 51 62	Excellent.	Acute Graves's disease. Amenorrhœa 3 months. 3.10.47, *Thyroideum Siccum*. Menses returned end November. 21.1.47, pulse 70, eyes normal, thyreoid barely palpable, menses regular. Feels splendid.

TABLE III.—*Continued.*

Class II.—Continued.

Case Number; Age (Years); Date Seen; Length of History.	Date.	Basal Metabolic Rate.	Weight in Pounds.	Pulse Rate per Minute.	Leucocytes per Cubic Millimetre.	Percentage of Neutrophile Cells.	Result.	Remarks.
42 Mrs. P.C. 35 years 29.10.46 2 years.	2. 9.46 18.11.46 9.12.46 20.1.47 10. 2.47	+26% +1% −8% −3% −22%	124 — 131 — 135	120 — 80 — 80	— 6,100 7,600 — —	— 42 51 — —	Excellent.	Had lost 21 lb. weight in a year. Final result apparently normal.
43 Mrs. N.C. 43 years 17.9.46 5 years.	26. 9.46 10.10.46 31.10.46 25.11.46 18.12.46 31. 1.47 18. 3.47	+54% +37% +14% +18% +3% −3% +1%	119 121 124 132 133 131 131	96 84 90 72 74 72 70	10,000 7,900 7,800 8,600 6,600 7,400 7,900	63 61 61 64 67 68 74	Excellent.	Treated with large doses of iodine for 3 months. Moderate exophthalmos. 25.11.46, *Thyroideum Siccum* gr. ½ b.d. 17.3.46, thyreoid only slightly noticeable, eyes normal. Feels very well.
44 Mrs. S.M.C. 31 years 2.10.46 1 year.	2.10.46 26.11.46 3.12.46 5. 2.47 4. 3.47 25. 3.47	+24% +5% — −12% +26% +3%	112 112 — 118 113 113	126 100 — 80 84 84	— 3,800 4,600 4,000 6,400 4,400	— 48 60 50 67 66	Good, but continuing.	In April, 1946, was given thiouracil 0·2 g. t.i.d. (but no adjuvant therapy) for 1 week and then 0·05 g. t.i.d. for 15 days. 7.2.47, *Thyroideum Siccum* gr. ½ b.d., but symptoms recurred and it was omitted 6.3.47. Clinically very well, but is still on maintenance dosage.
46 Mrs. G.C. 29 years 24.9.46 4 months.	—. 8.46 18.10.46 1.11.46 18.11.46 4.12.46 14. 1.47 11. 2.47	+34% +7% −12% −9% −33% −9% −9%	147 152 154 159 155 153 152	134 88 80 — 72 80 80	— — 9,000 6,000 9,000 — —	— — 72 50 70 — —	Excellent.	Very large hyperplastic goitre with prominent eyes. 5.12.46, *Thyroideum Siccum* gr. ½ b.d. 23.2.47, eyes normal, Thyreoid only just noticeable. Clinically normal.
47 Mrs. A.L.E. 29 years 21.1.47 1 year.	—.10.46 28. 1.47 10. 2.47	+54% +18% —	86 — —	120 — —	10,900 8,000 7,800	35 40 37	Febrile reaction. operated on.	Treated in South Africa with iodine and sedation. On tenth day of thiouracil therapy had rash and temperature of 99° F. Sent to hospital. On fifteenth day was given 0·05 g., 9 a.m. and 1 p.m. At 4 p.m. temperature 100° and at 8 p.m. 104·2° F. Was given iodine and operated on successfully.
49 Mrs. L.F. 33 years 8.5.46 1 year.	4. 6.46 2. 7.46 29. 7.46 12. 8.46 16. 9.46 22.10.46 5.12.46	+13% +2% −14% +2% +14% −3% +2%	151 157 157 157 162 171 —	120 82 — 84 96 86 72	7,100 — 8,300 5,600 7,700 7,000 6,800	42 — 48 60 69 66 60	Excellent.	Was given "Thyroidectin" for 5 months. Very large hyperplastic goitre and prominent eyes. 4.7.46, *Thyroideum Siccum* gr. ½ daily and 4 weeks later b.d. Note subsequent rise in B.M.R. Final result excellent, but thyreoid still obvious.
50 Mrs. E.M.F. 36 years 19.12.46 18 months.	23.12.46 6. 1.47 20. 1.47 3. 2.47 21. 2.47 17. 3.47	+69% +20% −1% −11% −14% −4%	112 — 118 — 120 125	106 — 72 96 72 84	— 7,500 7,300 6,100 — —	— 67 47 53 — —	Excellent.	Lost 35 lb. weight in 18 months. Very large thyreoid. 29.1.47, *Thyroideum Siccum* gr. ½ b.d. 3.3.47, thyreoid not altered. May require operation later for cosmetic reasons.
52 Mrs. E.M. 29 years 28.11.46 2 months.	18.12.46 5. 2.47 5. 3.47 19. 3.47	+45% +2% −12% +2%	143 181 183 187	140 76 90 72	10,700 9,500 5,200 6,000	67 53 57 57	Continuing.	In 1943 put on 28 lb. weight in 2 months and had B.M.R. +14%. Weight then 174 lb. In April, 1945, had a child. 10.5.45, B.M.R. +17%, thyreoid enlared with toxic symptoms. 29.4.46, B.M.R. +2%. Was given iodine and kept on until seen 28.11.46. 7.2.47, given *Thyroideum Siccum*.
53 Mrs. R.G.H. 36 years 10.5.46 3 months.	20. 5.46 7. 6.46 21. 6.46 23. 7.46 24. 9.46 26.11.46 14. 2.47	+31% +15% +13% −15% +6% +6% −5%	107 110 117 125 122 126 126	120 80 90 70 82 90 72	7,000 5,900 7,200 5,600 6,300 5,200 5,400	55 68 68 59 72 65 63	Excellent.	Although history of only 3 months was given it must have been longer. Had large hyperplastic thyreoid. 26.11.46, *Thyroideum Siccum* gr. ½ b.d., with slight improvement. Otherwise result excellent.
55 Miss M.J.H. 29.11.46 29 years 4 months.	15.11.46 17.12.46 21. 2.47 7. 3.47	+23% +20% −22% −19%	115 129 124 125	120 72 66 64	5,000 7,200 5,850 5,300	24 37 50 48	Excellent.	Note relative neutropenia. In the original count lymphocytes 59%, mononuclear cells 13%. 29.1.46, commenced *Thyroideum Siccum*.
59 Mrs. M.L. 29 years 30.5.46 3 months.	15. 3.46 30. 5.46 5. 7.46	+32% +24% −6%	133 135 140	110 100 90	— Reported as —	— normal. —	Excellent.	Was given large doses of iodine for 6 weeks after B.M.R. 15.3.46. Was then treated in hospital for 4 weeks, and after that by her own doctor. 31.1.47, clinically normal. Pulse 80.
61 Miss F.McL. 28 years 19.12.46 1 year.	12.12.46 7. 1.47 23. 1.47 20. 2.47	+59% +2% −13% −8%	121 129 132 135	120 — 72 80	5,700 6,100 8,000 6,800	63 56 57 61	Continuing.	Had typical hyperplastic thyreoid. 23.1.47, commenced *Thyroideum Siccum*, gr. ½ b.d.
63 Mrs. L.G. 34 years 1.8.46 2 years.	30. 4.46 5. 8.46 19. 8.46 9. 9.46 23. 9.46 8.10.46 28.10.46	+11% +11% +11% +8% −8% −14% −6%	107 109 — 112 113 115 115	90 96 — 90 80 66 68	— 8,400 8,700 10,000 15,200 8,400 7,900	— Reported as normal. 59 60	Excellent.	Treated with iodine since December, 1944, to August, 1946. Exophthalmos developed December, 1945, gradually increasing. In a highly emotional state, 16.5.46, when thiouracil was advised, but iodine was persisted with until 1.8.46. 20.3.47, apparently normal except for slight prominence of the eyes.

TABLE III.—*Continued.*

Class II.—Continued.

Case Number; Age (Years); Date Seen; Length of History.	Date.	Basal Metabolic Rate.	Weight in Pounds.	Pulse Rate per Minute.	Leucocytes per Cubic Millimetre.	Percentage of Neutrophile Cells.	Result.	Remarks.
64 Mrs. D.C.S. 30 years 1.11.46 6 months.	7.11.46 30.11.46	+20% −14%	140 143	110 82	4,800 6,100	56 74	Good.	Being treated by her doctor in the country. Has had a goitre for 6 years. Took thyreoid substance to reduce. Toxic symptoms developed over the last 6 months. Has been peculiar mentally. 25.2.47, physically well, but definitely psychotic.
70 Mrs. E.B. 36 years 8.2.47 18 months.	—.11.46 17. 2.47 3. 3.47 17. 3.47 31. 3.47	+31% +4% +8% −14% −17%	119 — — 124 —	136 72 76 72 76	— 4,100 5,900 4,100 5,150	— 59 49 55 52	Continuing.	A typical mild acute thyreotoxicosis, with hyperplastic gland. Apparently normal, but is to continue maintenance.
74 Mrs. D.McG. 30 years 11.2.47 6 months.	3.12.46 17. 2.47 3. 3.47 17. 3.47 1. 4.47	+27% +25% +18% ±0% −6	131 — — 134 135	96 — — 84 68	— 6,300 4,700 9,100 8,800	— 63 56 67 62	Continuing.	Was treated with iodine after first B.M.R. until 10.2.47. Is now on maintenance dosage. Apparently normal.
76 Miss M.O'C. 26 years 6 months.	24. 1.47 11. 2.47 25. 2.47	+25% +9% −2%	103 104 107	86 78 72	8,500 5,500 5,900	58 58 61	Continuing.	When first seen, conditions suggested a neurosis. On 3.3.47, appeared normal. Is on maintenance.
78 Miss L.K. 28 years 20.8.46 3 months.	20. 8.46 4. 9.46 14. 9.46 2.10.46 11.11.46 12. 2.47	+36% +9% +6% −18% −16% −14%	126 130 134 138 142 136	120 96 86 80 72 72	4,600 5,000 6,900 5,000 — 4,000	53 50 56 59 — 69	Excellent.	General malaise and melancholia at first suggested a neurosis. 28.2.47, appeared normal, felt splendid, and carrying on with heavy nursing duties.
80 Miss M.S. 37 years 16.7.46 3 months.	16. 7.46 1. 8.46 13. 8.46 17.9.46 10.10.46 6.11.46 24.12.46	+58% +9% −4% +13% +14% −6% −12%	107 110 117 117 117 116 118	144 — 84 90 — 72 70	4,500 5,600 4,000 5,000 9,300 5,200 4,600	60 72 60 64 — 52 51	Excellent.	Typical acute Graves's disease. 28.8.46, given *Thyroideum Siccum* gr. ½ b.d. As B.M.R. became elevated, dosage of methyl thiouracil was increased. Seen 26.3.47, pulse 70, thyreoid and eyes normal. Feels splendid.
81 Mrs. T.E.H. 40 years 7.2.47 3 years.	7. 2.47 5. 3.47 27. 3.47	+36% +6% −23%	105 114 116	150 100 66	6,000 12,600 6,600	55 68 67	Continuing.	Three years ago was in hospital for operation but was deferred. Baby 8 months ago, and acute symptoms recurred. Was in hospital and given iodine with thiouracil, but did not settle, and operation deferred. 7.2.47, when first seen, had large thyreoid. 27.3.47, *Thyroideum Siccum* gr. ½ b.d.
84 Mr. R.S. 26 years 25.2.47 3 months.	5. 3.47 19. 3.47 21. 4.47	+34% +3% −9%	134 145 151	140 90 72	5,500 5,000	35 54	Continuing.	Typical acute Graves's disease; responding well.

Class III. Over 45 Years. 18 Cases.

9 Mrs. E.H. 45 years 26.2.46 2 years.	26. 2.46 12. 3.46 26. 3.46 2. 5.46 25. 6.46 9. 8.46	+37% +21% −10% +3% ±0% +8%	132 135 133 137 139 145	160 100 76 80 100 90	9,500 11,100 9,100 8,000 8,800 8,400	62 56 63 56 69 66	Excellent.	Had been given iodine continuously for 14 months. B.M.R. +26% at commencement and +34% after 10 months. Had extreme tremor, nervousness *et cetera*, and lost 28 lb. weight. On 9.8.46 her condition appeared normal.
17 Mrs. G.M. 45 years 21.12.45 14 months.	5. 1.46 6. 2.46 21. 3.46 6. 5.46 4. 7.46 7. 8.46 4. 9.46 21.10.46 19. 2.47	+47% +9% −17% +1% +7% −1% −11% −19% −7%	129 135 142 140 139 139 138 138 132	120 96 78 80 90 92 72 66 72	7,600 4,900 5,800 7,800 6,300 6,000 6,500 5,000 7,200	50 50 41 44 63 53 47 46 53	Good.	Was seen February, 1945, with B.M.R. +42% and against advice her doctor gave large doses of iodine. May, 1945, B.M.R. +12%, but exophthalmos developed and progressed to such an extent that protective glasses were necessary. Toxicity was controlled by 21.3.46, but *Thyroideum Siccum* was given during a prolonged maintenance dosage of methyl thiouracil to try to control the exophthalmos. By February, 1947, the eyes were better, but obvious, and glasses had been discarded. General condition normal.
18 Mr. H.N. 48 years 11.2.46 1 year.	11. 2.46 6. 3.46 9. 4.46	+34% −8% −21%	200 216 218	96 72 70	5,400 6,550 6,000	56 51 (E. 10%) 40 (E. 1%)	Excellent.	Usual weight in training as a referee of wrestling, 17 stone. Became subthyreoid, but cleared in a few weeks on *Thyroideum Siccum* gr. ½ b.d. Resumed duties May, 1946, as was normal.
22 Mrs. L.W. 57 years 21.5.46 1 year.	21. 5.46 28. 6.46 12. 8.46 13. 3.47	+18% +8% −7% −7%	146 149 152 170	80 72 64 80	5,000 Reported normal.	49	Good.	Had a colloid goitre since a girl. In September, 1945, was given iodine, as had hypertension; B.M.R. +25%. Lost 21 lb. weight and developed tremor, lassitude *et cetera*. Difficult to assess because of the hypertension. After 4 weeks on methyl thiouracil felt well.

TABLE III.—*Continued.*

Class III.—Continued.

Case Number; Age (Years); Date Seen; Length of History.	Date.	Basal Metabolic Rate.	Weight in Pounds.	Pulse Rate per Minute.	Leucocytes per Cubic Millimetre.	Percentage of Neutrophile Cells.	Result.	Remarks.
23 Mrs. L.M.Bks. 53 years 19.2.46 18 months.	19. 2.46 5. 3.46 26. 3.46 2. 4.46 14. 5.46 29. 7.46	+54% +18% +11% ±0% +26% −23%	113 114 124 133 147 155	150 100 84 80 130 52	7,200 3,700 6,800 7,600 7,300 5,500	56 54 48 59 51 65	Good.	Had enlarged thyreoid 18 months, with toxicity, but much worse after pneumonia 8 months ago. Fibrillating; œdema of legs; exophthalmos marked. After 4 weeks normal heart rhythm. *Thyroideum Siccum* given 20.3.46, but ceased 14.5.46 because of reaction. Seen December, 1946, and was well except for enlarged thyreoid and prominent eyes. Pulse 76.
35 Mrs. A.M.S. 52 years 26.4.46 8 months.	26. 4.46 22. 5.46 4. 6.46	+14% +9% +9%	100 102 108	120 80 72	7,600 6,800 —	58 57 —	Excellent.	Treated with large doses of iodine for 6 months. Hard enlarged thyreoid and prominent eyes. Treated in country under direction. Seen 25.10.46: apparently normal. Pulse 70.
32 Mr. E.C. 47 years 17.7.46 6 months.	17. 7.46 24. 7.46 7. 8.46 21. 8.46 4. 9.46 25. 9.46 16.10.46 15.11.46	— +27% +25%? +17% +5% −30% −6% +4%	160 169 165 164 176 182 165 163	120 78 82 72 70 72 84 80	7,600 9,000 8,800 6,200 7,600 7,500 5,600 8,700	71 61 69 85 74 43 71 63	Excellent.	Acute hyperplastic toxic goitre, so treatment was begun at once, 17.7.46. On 30.7.46 ran out of tablets, and had none for 10 days. Clinical response was better than indicated by B.M.R. On 6.2.47 eyes and thyreoid normal and felt splendid. On 25.9.46, given *Thyroideum Siccum* gr. ½ b.d. for 3 months.
36 Mrs. A.S. 51 years 11.7.46 6 months.	11. 7.46 3. 9.46 22. 1.47	+34% −6% −15%	124 124 124	132 84 84	— 5,300 5,400	— 59 60	Excellent.	Had hypertension with an acute hyperplastic toxic goitre. Appeared normal, 28.2.47, except for raised blood pressure.
51 Mr. J.G. 46 years 14.10.46 2 years.	14.10.46 28.10.46 11.11.46 25.11.46 20. 2.47	+29% +13% +9% −30% +17%	132 136 136 138 139	110 84 72 64 78	7,300 8,200 7,400 6,900 —	69 62 61 (E. 7%) 72 —	Good.	Had been on iodine for 3 months. Very enlarged gland and marked exophthalmos. Very restless. 25.11.46, put on *Thyroideum Siccum*. Gland had subsided except for an adenoma of right lobe. Operation was advised. Otherwise appeared normal on 17.3.47. The raised B.M.R., 20.2.47, was reaction to *Thyroideum Siccum*.
54 Mrs. E.H. 45 years 7.8.46 3 months.	7. 8.46 21. 8.46 4. 9.46 18. 9.46 10.10.46 25.10.46 29. 1.47	+37% +18% +18% +25% +3% −5% −3%	180 174 174 172 172 175 181	140 92 84 102 84 72 72	6,400 6,600 7,900 6,400 6,500 8,700 —	45 54 54 43 34 (E. 5%) 62 —	Excellent.	Acute hyperplastic toxic goitre with prominent eyes. Ran out of tablets, 12.9.46, and could not get any more until 25.9.46. Note consequential rise in B.M.R. Final result apparently normal.
57 Mrs. I.M.K. 47 years 30.3.46 3 years.	30. 3.46 6. 5.46 21. 6.46 5. 9.46 17.10.46 26. 2.47	+25% +19% +6% +6% −12% +2%	126 126 138 137 140 150	110 84 74 70 70 64	8,000 8,000 8,000 7,600 — —	73 72 68 70 — —	Excellent.	Treated with iodine for 15 months. Large hard gland and prominent eyes. Started on *Thyroideum Siccum* 5.7.46. On 7.10.46 had diplopia and paresis of right inferior oblique. 19.3.47, apparently normal; gland not palpable.
83 Mrs. E.W.P. 54 years 29.1.47 3 years.	29. 1.47 18. 2.47 4. 3.47 12. 3.47	+15% +14% +14% −11%	130 136 140 145	72 92 72 70	6,100 6,800 6,500 7,000	44 (E. 5%) 46 (E. 8%) 60 (E. 3%) 55 (E. 4%)	Continuing.	Chronic thyreotoxicosis with small thyreoid gland. Fibrillating.
58 Mrs. W.M.K. 58 years 9.10.46 3 years.	9.10.46 18.10.46 1.11.46 18.11.46 3.12.46 21. 2.47	+25% +19% +2% −2% −6% −8%	128 131 133 137 140 142	144 78 62 80 66 68	— 7,500 6,200 6,100 5,700 8,300	— 56 40 (E. 4%) 49 52 58	Good.	Had left eye prominent for 3 years and in last 2 years an enlarged thyreoid gland. 20.11.46, commenced on *Thyroideum Siccum*. 28.2.47, thyreoid normal, but left eye still prominent.
60 Mrs. L.M.M. 54 years 29.10.46 1 year.	1.11.46 18.11.46 6.12.46 31. 1.47 27. 3.47	+28% +7% −2% −9% −12%	109 108 119 122 125	110 76 74 78 80	6,000 6,800 7,200 6,200 7,000	58 (E. 4%) 65 (E. 4%) 61 (E. 1%) 45 (E. 4%) 50 (E. 5%)	Excellent.	Typical acute hyperplastic toxic goitre. 9.12.46, given *Thyroideum Siccum*. 29.3.47, apparently normal.
62 Mrs. E.R. 48 years 8.5.46 1 year.	22. 4.46 23. 5.46 7. 6.46 21. 6.46 24. 7.46 21. 8.46 2.10.46 31.10.46 18. 2.47 13. 3.47	+40% +44% +32% +26% +20% +17% +10% +7% +13% +9%	116 — 116 115 117 116 115 111 113 115	132 — 110 108 100 84 86 96 94 90	— 5,600 5,700 4,500 8,400 5,300 6,900 5,600 4,400 5,600	— 58 54 55 67 55 59 49 62 70	Continuing.	Was treated with large doses of iodine for some 6 months or more. A very slow response, although clinically satisfactory. In error, omitted the methyl thiouracil, 12.11.46 to 20.2.47, but took the *Thyroideum Siccum*.

TABLE III.—*Continued.*
Class III.—Continued.

Case Number; Age (Years); Date Seen; Length of History.	Date.	Basal Metabolic Rate.	Weight in Pounds.	Pulse Rate per Minute.	Leucocytes per Cubic Millimetre.	Percentage of Neutrophile Cells.	Result.	Remarks.
65 Mrs. E.S. 51 years 5.11.46 3 months.	5.11.46 20.12.46 10. 1.47 31. 1.47	+23% −18% −12% −11%	139 — — —	110 — — —	— 6,000 6,000 4,000	— 70 (E. 7%) 58 (E. 2%) 63 (E. 5%)	Continuing.	Onset after brother killed in an accident. Had marked left exophthalmos. Treated under direction. 7.1.47, *Thyroideum Siccum* commenced. 19.2.47, eye much better. Generally very well. Pulse 84.
73 Mrs. N.M. 47 years 20.1.47 18 months.	20. 1.47 26. 2.47 12. 3.47	+32% −4% −16%	133 138 143	120 80 72	— 6,900 7,100	— — —	Continuing.	Acute hyperplastic toxic goitre. Treated by her own doctor under direction.
82 Miss K.B. 46 years 13.1.47 4 months.	13. 1.47 11. 2.47 18. 2.47	+35% +7% −15%	104 108 112	140 90 68	7,200 — 5,900	65 — 65	Continuing.	Acute hyperplastic toxic goitre. 20.3.47, commenced *Thyroideum Siccum*.
				Class IV. Adenoma. Nine Cases.				
7 Miss P.D.F. 49 years 7.9.45 1 year.	7. 9.45 25. 9.45 9.10.45 17.11.45 23. 1.46 11. 4.46 2. 6.46	+13% +2% −16% +18% −16% +8% −10%	108 112 119 118 122 122 124	88 80 80 120 80 72 84	7,650 9,000 7,900 7,000 7,600 7,000 —	77 68 61 65 70 68 —	Fair.	Was referred for operation 2.11.45, but as the hippuric acid excretion was only 44% of normal, operation was deferred. As eyes were prominent and thyroid had enlarged, was given *Thyroideum Siccum*, which caused elevation of B.M.R. In October, 1946, hippuric acid excretion was 79%, but she refused operation. Is carrying on well with small maintenance doses.
26 Mrs. L.P. 36 years 12.2.46 8 months.	11. 2.46 26. 2.46 12. 3.46 26. 3.46 9. 4.46	+75% +36% +24% −1% +1%	88 93 105 110 115	140 130 — 100 —	— 9,300 7,100 9,100 8,800	— 63 62 51 56	Fair.	Multiple adenomatous thyroid. Was admitted to hospital for operation in May, 1946, but wished it deferred. To carry on with small maintenance doses.
27 Mrs. E.M.S. 51 years 8.3.46 2 years.	8. 3.46 26. 3.46 2. 4.46 24. 4.46	+33% +14% — —	113 115 — —	110 100 — —	5,000 8,000 8,000 6,200	66 (E. 11%) 50 (E. 18%) 52 (E. 24%) 49 (E. 19%)	Operation.	Symptoms came after severe nasal hæmorrhage 2 years ago necessitating transfusion, which was followed by an exfoliative dermatitis. Treated since with iodine. Severe epistaxis recurred 2 weeks ago, has been very ill since. Fibrillating. Given transfusion. Started on methyl thiouracil, but exfoliative dermatitis ensued. Operated on 27.5.46, total thyreoidectomy. Did very well and was apparently normal in August, 1946.
45 Mrs. C.C. 61 years 11.10.46 4 months.	11.10.46 31.10.46 21.11.46 23.12.46 17. 2.47	+35% +16% +12% +8% +1%	151 150 152 — —	110 84 72 84 —	7,500 5,100 6,000 4,600 5,200	75 (E. 3%) 69 (E. 1%) 70 (E. 4%) 59 (E. 10%) 63	Fair.	Enlarged thyreoid noticed after an attack of acute biliary colic 4 months ago, and has since lost 35 lb. weight. Has hypertension, enlarged heart, para-œsophageal hernia of stomach, multiple diverticulosis of jejunum, and a calculus in right kidney. Multiple adenomatous thyreoid.
56 Mrs. L.J. 58 years 4.12.46 1 year.	20.12.46 16. 1.47 24. 2.47 21. 3.47	+20% +1% +1% +20%	91 95 98 101	132 110 102 96	3,400 4,100 5,600 7,100	58 54 58 54	Continuing.	Multiple adenomatous thyreoid for 28 years, but toxicity only 1 year. Operation advised February, 1947, but refused. Note recrudescence, March, 1947, following domestic worries, also corneal ulcer developed. Operation again advised, but refused.
66 Mrs. I.T. 52 years 6.8.46 4 years.	20. 8.46 2. 9.46 16. 9.46 30. 9.46 30.10.46 10. 3.47	+20% +6% +11% +18% +11% +22%	109 113 114 115 115 123	112 72 72 78 72 68	9,100 8,400 9,000 8,200 10,100 —	71 70 64 82 68 —	Continuing.	Adenomatous thyreoid for 29 years. Toxicity followed operation for acute intestinal obstruction 4 years ago. Eyes prominent and very large thyreoid. Given *Thyroideum Siccum* 30.9.46 until 10.3.47: eyes normal, no change in thyreoid. Operation refused.
67 Miss M.F.R. 33 years 25.7.46 1 year.	2. 8.46 16. 8.46 30. 8.46 13. 9.46 27. 9.46 30.10.46 23. 2.47 10. 3.47	+20% +16% ±0% −4% +8% +2% +37% +34%	106 110 113 114 114 111 100 102	84 72 92 72 84 80 108 72	9,700 8,100 11,700 — 11,600 8,500 8,700 —	63 62 76 (E. 2%) — 69 (E. 3%) 52 (E. 4%) 55 (E. 11%) —	For operation.	In May, 1946, had B.M.R. +38%. Thyreoid very large and nodular. Eyes very prominent. 17.9.46, given *Thyroideum Siccum* until relapse occurred at end of January, 1947. Eyes normal and thyreoid smaller. 25.3.47, definite adenoma of right lobe now evident. Operation advised and agreed to after 3 weeks on iodine.
68 Mrs. M.K. 64 years 27.8.46 1 year.	7. 8.46 10. 9.46 24. 9.46 8.10.46	+39% +37% +11% −9%	117 125 — —	120 90 — —	7,800 6,000 8,000 —	60 65 — —	Fair.	Adenomatous thyreoid for many years. Toxicity one year. In November, 1946, had a recurrence of psoriasis and ceased further treatment. Seen 7.3.47: pulse 84, feels very well, thyreoid not altered.

TABLE III.—*Continued.*

Class IV.—Continued.

Case Number; Age (Years); Date Seen; Length of History.	Date.	Basal Metabolic Rate.	Weight in Pounds.	Pulse Rate per Minute.	Leucocytes per Cubic Millimetre.	Percentage of Neutrophile Cells.	Result.	Remarks.
71 Mrs. C.M.B. 71 years 21.1.47 6 months.	5. 2.47 19. 2.47 5. 3.47 19. 3.47	+11% +9% −2% +12%	154 — — 157	96 80 70 96	5,500 5,700 4,800 6,400	46 (E. 5%) 42 (E. 2%) 51 (E. 6%) 59 (E. 2%)	Continuing.	Adenomatous thyreoid for many years. Has hypertension and cholelithiasis.
Class V. Recurrent. 10 Cases.								
1 Miss M.B. 28 years 28.12.45 3½ years.	24.12.45 31. 1.46 1. 3.46	+24% −2% −17%	124 127 131	140 120 108	6,000 5,600 8,000	77 79 74	Excellent.	X-ray therapy, 1943, and then iodine. June, 1945, B.M.R. +14%: symptoms recurred in last 6 months. Seen 13.2.47: apparently normal.
10 Mr. J.H. 64 years 20.1.46 3 years.	16. 1.46 31. 1.46 27. 3.46 7. 5.46 2. 8.46	+38% +18% −7% −17% −8%	126 134 171 165 177	140 100 84 72 76	7,000 7,400 5,500 5,400 —	56 54 61 55 —	Excellent.	April, 1944, B.M.R. +25%. Medical treatment and three courses of X-ray therapy. In June, 1945, B.M.R. +41%. Seen 20.1.46: fibrillating, losing weight, unable to work for last 18 months, most of which was spent in hospitals. Fibrillation controlled after 4 weeks. Returned to active work, April, 1946. Seen 15.3.47: very well, weight 181 lb., occasional slow fibrillation.
11 Mrs. I.M.J. 57 years 28.12.45 1 year.	21.12.45 16. 1.45	+26% −6%	120 122	110 72	7,000 6,500	68 63	Excellent.	Deep X-ray therapy 8 months ago. Returned to country in January, 1946, on maintenance dosage. Seen 24.9.46: apparently normal. Went through a big pelvic operation in June, 1946, without any trouble.
19 Mr. K.P. 33 years 15.12.45 4 years.	21.12.45 19. 1.46	+12% +10%	131 143	84 80	5,900 5,500	39 43	Excellent.	Right hemithyreoidectomy 4 years ago. Well for 9 months, then relapsed and much worse in the last year. Large left lobe now. Treatment continued in country. May, 1946, apparently normal and gland regressed.
31 Mrs. E.M.B. 33 years 11.4.46 2½ years.	8. 4.46 14. 5.46 1. 7.46 21. 8.46	+36% +8% −4% −7%	132 140 147 143	96 80 100 90	7,900 10,100 — —	56 56 — —	Excellent.	Had subtotal thyreoidectomy, 6.2.46, for large hyperplastic goitre. Never got really well. Final result December, 1946, apparently normal.
38 Mrs. E.E. 35 years 21.1.47 2 years.	21. 1.47 13. 2.47 22. 2.47 28. 2.47	+17% +12% — +17%	116 117 — 119	160 120 — 90	3,900 2,500 4,000 3,700	58 51 62 77	Referred for X ray.	Operation, 1939. Symptoms recurred in 1942 with very enlarged gland. Had two courses of X-ray therapy. Had diarrhœa and ulcerated mouth, with a leucopenia. Sent for further X-ray treatment, 13.2.47.
40 Mrs. F.M.B. 61 years 18.7.46 2 years.	19. 7.46 5. 8.46 18. 9.46	+15% −2% −1%	112 116 122	120 84 72	5,800 7,000 5,100	43 (E. 4%) 54 (E. 2%) 53 (E. 2%)	Good.	X-ray treatment February, 1945; had severe reaction and a mental breakdown. Hippuric acid excretion, 49%. Seen 10.12.46: pulse 80, weight 125 lb., condition good.
69 Mrs. E.B. 50 years 15.11.46 3 years.	3.10.46 17.12.46 20. 1.47	+27% −8% −7%	164 — 163	108 — —	— — 7,600	— — 69	Continuing.	In October, 1943, B.M.R. +50%. Had three courses of deep X-ray therapy up to December, 1945. In May, 1945, B.M.R. −19%. In March, 1946, was fibrillating and very ill—had two months in hospital. 9.6.46, B.M.R. +14%. When seen November, 1946, fibrillating. No palpable thyreoid. On 18.3.46, fibrillation, pulse 72, very well.
75 Mr. A.McI. 53 years 13.2.47	6. 2.47 28. 2.47	+12% −15%	145 150	90 84	3,800 6,000	48 (E. 7%) 53 (E. 12%)	Continuing.	Treated by deep X ray and radium collar 12 years ago for acute thyreotoxicosis; had B.M.R. +50% well up to 4 months ago and all acute symptoms recurred with fibrillation. 23.3.47, put on weight 28 lb., pulse 70, and feels normal.
79 Mrs. H.V. 30 years 3.2.47 18 months.	3. 2.47 21. 2.47 21. 3.47	+15% −2% +6%	120 123 124	108 96 74	7,200 5,200 8,600	73 67 66	Continuing.	In November, 1945, to January, 1946, treated in hospital in England, and again in February, 1946. Had deep X-ray therapy. Never felt well, and had all usual toxic manifestations.

recurrences would be rare." This latter remark is very true, except that it is not necessary to induce a true clinical myxœdema but rather a hypothyreoidism short of such a state. They sum up by stating: "Any drug which is as safe as a surgical operation and which can obtain the same ends without incurring discomfort and occasional morbidity is a better therapeutic measure than surgery."

In the literature a definite tendency is being expressed in many clinics to regard thiouracil as a possible cure in many cases of thyreotoxicosis, but apparently many clinics do not differentiate clearly enough between the nodular (adenomatous) and non-nodular (hyperplastic) toxic goitres. Bierwalter and Sturgis are definite about it. Also the principle of minimal dosage has not been generally

adopted, but R. H. Williams mentions that in his last 150 cases the dose in the majority has not exceeded 0·5 gramme per day. It is evident that a suitable maintenance dose must be carried on for several months, and it has been mentioned that when this is done patients do not relapse in the same proportion as those who have had short-term therapy. It does not seem to have been recognized, however, that during this maintenance period the basal metabolic rate must be kept at zero or preferably at a *minus* level.

Some Case Reports.

A Case of Relapse after Methyl Thiouracil Therapy.

CASE 13 (Class II).—Mrs. S.McL., aged thirty-seven years, first seen on February 28, 1946, had a three-year history mainly of fluctuation in weight, but had become very nervy in the previous six months, and the full clinical picture of acute thyreotoxicosis developed with moderate exophthalmos and a large hyperplastic thyreoid. She was started at once on methyl thiouracil, and on March 6, 1946, the basal metabolic rate was + 46%, the pulse rate 120, and the weight seven stone. The basal metabolic rate fell to zero on May 1, 1946, although *Thyroideum Siccum* was started on April 8, 1946, as the eyes were more prominent and also the thyreoid. Treatment was discontinued on November 29, 1946, when she appeared normal and stated that she "felt better than for many years". Her pulse rate was 76 and her weight six stone eleven pounds. She remained well until the middle of February, 1947, when the thyreoid enlarged and the pulse rate became rapid. On March 6, 1947, the basal metabolic rate was + 29% and the pulse rate 94; the administration of methyl thiouracil was resumed. When seen on April 1, 1947, she expressed herself as feeling quite right again. Her pulse rate was 80 in the minute. The thyreoid was slightly enlarged and the eyes were full.

Treatment was continued and it looks as if she will keep well on a low maintenance dose of 0·05 gramme which will be continued for three or four months.

A Case of Relapse after Thiouracil Therapy.

Mr. F.W., aged thirty-nine years, was first seen on August 31, 1945. He had typical acute thyreotoxicosis of some three months' duration. He desired operation and was sent into hospital, but the result of his hippuric acid excretion test was only 48%, showing gross impairment of the detoxicating function of the liver, and operation would have been fatal. He was given thiouracil and adjuvant treatment.

The initial basal metabolic rate was + 38% and fell to − 10% by October 30, 1946, but his hippuric acid excretion had risen to only 53%, so operation being definitely excluded he was discharged from hospital to carry on with thiouracil. This was discontinued on May 27, 1946, when he had a basal metabolic rate of − 3% and appeared normal.

He remained well until the middle of December, 1946, when acute symptoms recurred and on January 16, 1946, the basic metabolic rate was + 17%, so methyl thiouracil was ordered. He settled quickly and his basic metabolic rate on February 28, 1947, was only + 2% and he felt well again. He was given *Thyroideum Siccum* then as the thyreoid gland was enlarged. On March 25, 1947, his basic metabolic rate was − 24%, his pulse rate was 76, the thyreoid gland was barely noticeable and he had regained his usual weight and well-being. It was decided to carry on with 0·05 gramme doses twice daily and with the *Thyroideum Siccum* for another six to eight weeks.

A Case of Agranulocytosis with Methyl Thiouracil.

Mrs. B.R., aged forty-two years, was seen in consultation on March 13, 1947. The onset of her illness was in November, 1945, when the right eye became prominent and a few months later the left eye followed suit. She was seen by her doctor in October, 1946. The basic metabolic rate was + 36% and the pulse rate only 80 per minute; there was no apparent enlargement of the thyreoid gland. The leucocyte count was 9,400 per cubic millimetre with 48% neutrophile cells.

Methyl thiouracil 0·2 gramme was given three times a day on October 15, 1946, for ten days and then twice a day. Early in November the whole family had influenza, as did the patient, but on November 16, 1946, she had a temperature of 100° F. with an apparent follicular tonsillitis. The leucocytes were then 2,100 per cubic millimetre with no sign of granulocytes, there being 89% lymphocytes and 11% mononuclear cells. The red cell count was 3,700,000 per cubic millimetre with 54% hæmoglobin value. She was admitted to hospital and given penicillin and injections of liver, being discharged after six weeks.

On March 4, 1947, the basic metabolic rate was + 24% and the leucocyte count 7,600 per cubic millimetre with 53% neutrophile cells and 2% eosinophile cells. The red cell count was 4,200,000 per cubic millimetre and the hæmoglobin value was 81%. When she was referred for consultation, the pulse rate was 102, she had a small firm thyreoid gland and there was definite exophthalmos of the right eye and slightly also of the left eye.

The administration of mixed vitamin therapy was ordered with added vitamin *B* group and deep *X*-ray therapy was advised.

A Case of Resistance to Thiouracil.

Mrs. P.M., aged forty years, had treatment which was commenced in January, 1946. Thiouracil 0·05 gramme was given three times a day and a week later 0·2 gramme was given three times a day continuously until October, 1946, when it was changed to methyl thiouracil 0·2 gramme three times a day.

The patient had been ill and under sedation for two years prior to this. Her weight had fallen from eight stone ten pounds to six stone five pounds. Slight thyreoid hyperplasia only was present, but exophthalmos was very evident. She was a very sick woman and was sent to hospital to initiate treatment.

On February 8, 1946, the basic metabolic rate was + 66%, the leucocyte count was 5,000 per cubic millimetre, the neutrophile cells being 43% and the eosinophile cells 14%. On February 14, 1946, the basic metabolic rate was + 45%, the leucocyte count was 6,000 per cubic millimetre, the neutrophile cells being 49% and the eosinophile cells 10%. On June 3, 1946, the basic metabolic rate was + 14%, the leucocyte count was 9,800 per cubic millimetre, the neutrophile cells being 66% and the eosinophile cells 4%. On September 3, 1946, the basic metabolic rate was + 34%, the leucocyte count was 7,400 per cubic millimetre, the neutrophile cells being 57% and the eosinophile cells 9% (the basic metabolic rate was very doubtful). On February 14, 1947, the basic metabolic rate was + 0%, the leucocyte count was 6,800 per cubic millimetre, the neutrophile cells being 63% and the eosinophile cells 4%.

The patient was first seen by me on March 31, 1947. She had a very large hyperplastic gland which had developed during treatment. She had amenorrhœa from December, 1944, to April, 1945, and again from December, 1945, to April, 1946, but had been regular in the last summer. She was seen by a physician in October, 1946, who advised operation. Apart from sedation she had no adjuvant therapy. She developed asthma shortly after the onset of treatment, but this declined and she had none of the usual toxic reactions.

It would probably have been wiser to have increased the dosage about March, 1946, or to have submitted her to operation about June.

The basal metabolic rate of September 3, 1946, of + 34% was probably incorrect, and the biochemist queried it and suggested that the estimation should be repeated a week later, but this was not done. The leucocytes remained at a high level all along with eosinophile cells always present. The initial eosinophilia indicated some probable anaphylactic state as evidenced later by the onset of asthma.

Advice given was to retain the dosage of 0·2 gramme of methyl thiouracil along with *Thyroideum Siccum* half a grain twice a day and potassium iodide two grains twice a day, also "AktaVite" one teaspoonful three times a day, and to have the basal metabolic rate determined in four weeks when the condition could be reviewed as to the advisability of operation.

Conclusions.

Further experience with both thiouracil and methyl thiouracil confirms on the whole the conclusions arrived at in the article published in THE MEDICAL JOURNAL OF AUSTRALIA of December 7, 1946, and they may be repeated with minor modifications as follows:

1. Methyl thiouracil is superior to other "thio" preparations in the treatment of thyreotoxicosis.

2. The minimal dose which will produce the desired effect is the safest dosage.

3. Each patient presents an individual problem and requires constant supervision during the whole course of treatment.

4. The major factor in securing permanency of control of thyreotoxicosis is the maintenance of a zero or *minus* metabolic rate for four months before cessation of treatment.

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5. Adjuvant therapy in the form of sedation, mixed vitamin therapy and adequate balanced diet is necessary.

6. A high protein diet is necessary if there has been any undue loss of weight or muscle wasting.

7. Regular leucocyte counts are imperative, and if possible estimations of the basal metabolic rate for the first six to eight weeks are advisable. Follow-up should be carried out for six months after treatment is suspended.

8. The minimal period of treatment should be five months if no *Thyroideum Siccum* has been given, and if so it should be six months.

9. The best results are obtainable in cases of acute hyperplastic toxic goitre, and the earlier the patients come to treatment, the more satisfactory is the final result. Present figures indicate that apparent cure can be obtained in 88% of cases when the technique as outlined is followed faithfully.

10. Gland hyperplasia and exophthalmos of moderate degree can be cleared in most cases of not more than four months' duration by the administration of *Thyroideum Siccum* during the maintenance period of dosage.

11. Patients with toxic adenomatous goitre do not respond satisfactorily to this form of treatment, and if operable should be advised to have surgical treatment as soon as control of toxicity is secured. It is necessary in all such cases to have a Quick's hippuric acid excretion test carried out to determine the detoxicating function of the liver which is depressed in so many of these cases, rendering operation a risky procedure.

12. The previous administration of iodine doubles the average time to secure "adequate response" and lengthens the total period of time for treatment.

13. Mild idiosyncratic reactions may occur, but seldom necessitate suspension of treatment for more than twenty-four to forty-eight hours.

14. Febrile reactions should be regarded as a warning of a more severe toxic reaction. Leucopenia should also be regarded with suspicion, as agranulocytosis, although rare, must always be kept in mind.

15. Only two cases of relapse some months after cessation of treatment have been observed—one with thiouracil and one with methyl thiouracil, that is, less than 2% in the combined total.

16. Misuse of "thio" drugs is still found, and they should not be ordered without a proven diagnosis of thyreotoxicosis as they are valueless in neuroses which may mimic thyreotoxicosis closely.

Acknowledgements.

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I am indebted to the librarians of the Gordon Craig Library of the Royal Australasian College of Surgeons for advice as to relevant articles in current medical literature and to the librarian of the library of the New South Wales Branch of the British Medical Association, Sydney, for securing journals for me. To my secretary, Mrs. Thorpe, I wish to offer my thanks for her meticulous care in the preparation of this article.

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CHRONIC SUBDURAL HÆMATOMA, SO-CALLED.

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THE subject of subdural hæmorrhage has aroused the interest of clinicians and pathologists for a very long time past. A most instructive historical review is to be found in a paper by Putnam and Cushing[1] published in 1925. Many reports dealing with the surgery of "subdural hæmorrhage" appeared in the latter part of the nineteenth century, and a valuable review of these was undertaken by Bowen,[2] his paper being published in the year 1905. In many of the cases reported the hæmorrhage was sufficient to cause grave symptoms within a short time of the injury; but Bowen pointed out that often there was a very long "lucid interval" before the onset of serious symptoms. There is little doubt that some examples of what would now be called chronic subdural hæmatoma were included. Trotter[3] in 1914 published a paper in which he reported four cases of "chronic subdural hæmorrhage". His description of the clinical features of the condition in question was accurate and left little to be added up to the present time. Since 1914 scores of papers have appeared dealing with the subject of chronic subdural hæmatoma in its various aspects; but many problems still await solution.

The usually accepted theory of the formation of subdural hæmatoma is that advanced by Trotter. He supposed that an injury caused tearing of a vein passing from the cortex of the brain to the *dura mater* in the region of one or other of the venous sinuses, with effusion of blood into the subdural space.[1] This blood he supposed then to become enclosed between a new membrane which formed beneath and in contact with the *dura mater* and another thin membrane which lay on the deep aspect of the blood, in contact with but distinct from the arachnoid membrane. Trotter suggested that chronic internal hæmorrhagic pachymeningitis and blood cysts associated with this condition were caused by trauma in the same way.

Hannah[4] held that the hæmorrhage was not subdural but intradural in situation. Other authors,[5][6] whilst admitting the possibility that blood effused into the subdural space may result in the formation of a chronic hæmatoma, agree with Hannah in the main. Their views do not seem to have received due recognition.

[1] Ford Robertson had previously suggested this source of bleeding in his book "Pathology of Mental Disease", published in 1900.

It is the purpose of the writer in this paper to adduce support for Hannah's theory and further to suggest that true subdural hæmorrhage does not give rise to "chronic subdural hæmatoma".

Evidence in Favour of an Intradural Situation of the Hæmatoma.

1. The inner limiting membrane is formed, as was pointed out by Hannah,[4] of adult cells indistinguishable from those of the inner layer of the *dura mater*, with which it is continuous. It is scarcely conceivable that in a few weeks a membrane composed of newly formed cells could attain to this structure. The appearance is such as to suggest most forcibly that hæmorrhage has taken place into the delicate vascular layer of the *dura mater*, which lies between its innermost thin fibrous layer and the thicker fibrous layers which make up the body of the membrane. The innermost layer thus split off from the rest of the dura becomes the inner limiting membrane of the hæmatoma.

2. In the *dura mater* beyond the limits of a hæmatoma there are frequently to be seen small satellite collections of blood. These have membranes similar in all respects to those of the main collection. It is easy to imagine that if several of these small hæmorrhages increased in size and ran together, a major hæmatoma would result. On the other hand, it is scarcely to be supposed that multiple encapsulated hæmatomata could form as the result of effusion of blood into the subdural space.

3. Chronic "subdural" hæmatomata are found almost exclusively over the convexity of the cerebrum; the writer has not seen an undoubted example of a hæmatoma in any other situation or any illustration of such a condition. Subdural hæmatomata seldom extended below the level of the Sylvian fissure. It was recognized by pathologists of the nineteenth century that *pachymeningitis hæmorrhagica interna* commonly affected the *dura mater* in the same situation. It is hard to conceive of a bulky hæmorrhage into the subdural space over the convexity of a hemisphere which would not extend to the base of the brain, and in practice this is found to occur. There is usually a good depth of blood below the Sylvian region and under the temporal lobe.

4. Chronic subdural hæmatoma is found on both sides in a large proportion of cases—from 30% to 40% according to some authors. But chronic subdural hæmatoma is a rather uncommon condition and it seems therefore that only very rarely would two occur simultaneously in the one person. To account for such an occurrence in terms of the theory of origin which supposes that hæmorrhage takes place into the subdural space with subsequent encapsulation, it would be necessary to assume that two separate effusions of blood occurred, one over the convexity of each hemisphere; that the blood in each case failed to take the course usually followed by blood in this situation—to wit, downwards into the Sylvian region and the middle fossa of the skull; and further, that instead of either destroying the patient or being removed in the course of time by absorption, not one but both effusions became encapsulated to produce "chronic hæmatomata". This surely is difficult of belief. On the other hand, it is not difficult to explain the high frequency of occurrence of two hæmatomata in the one person if it is supposed that there is some individual peculiarity or weakness of the *dura mater* or its vessels which renders it liable to hæmorrhage into the vascular layer.

Does Chronic Subdural Hæmatoma ever Develop as a Result of True Subdural Hæmorrhage?

If it is conceded that chronic hæmatomata do form in the *dura mater*, then it would seem to be unlikely that an identical hæmatoma would ever form in another situation, such as the subdural space. Attempts to produce chronic subdural hæmatomata in animals by introducing blood into the subdural spaces have not been successful, according to Baker.[6] Hæmorrhage into the subdural space occurs commonly as a result of trauma; but in the huge majority of such cases no chronic hæmatoma develops.

As has been pointed out above, blood effused into the subdural space does not commonly, if ever, become localized in the area in which subdural hæmatomata are almost invariably found. If it is supposed that a true subdural collection of blood situated in the region in which subdural hæmatomata are usually found may become encapsulated to form a chronic hæmatoma, then there would seem to be no good reason why collections of blood which are known to occur commonly in other situations should not behave similarly. In point of fact they do not.

Summary and Conclusions.

An attempt is made to support the view advanced by Hannah that "subdural hæmatomata" are not in fact situated beneath the *dura mater*, but in it.

The name subdural hæmatoma should be dropped in favour of *hæmatoma duræ matris*, as suggested by Hannah.

It is suggested that true subdural hæmorrhage does not give rise to "chronic subdural" hæmatoma.

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Reports of Cases.

BAL THERAPY IN ACUTE ARSENICAL POISONING AND GOLD INTOXICATION.

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THE substance BAL—British Anti-Lewisite—was evolved during the recent war as a counter to the possible use of Lewisite gas; since the termination of hostilities it has been used experimentally and in clinical medicine, in the treatment of systemic poisoning with heavy metals, and in the treatment of the complications arising from their use.

Two patients respectively suffering from acute arsenical poisoning and acute exfoliative dermatitis following the use of "Myocrisin" were recently admitted to the Royal Prince Alfred Hospital, and the drug BAL was used in the treatment of each with strikingly successful results.

In view of the fact that as yet no mention has been made of the clinical application of BAL in the Australian literature, the cases are considered worthy of being reported; further, a dosage has been indicated and the possible side effects are recorded. In the following cases no side effects were observed.

Arsenical poisoning is not a common condition nowadays, and the acute variety is rarely encountered. The records of the Royal Prince Alfred Hospital contain reports of twelve cases of poisoning due to arsenic during the period from 1930 to 1945. The arsenical compounds used were various types of insecticides, chiefly paris green, which was responsible for four cases in the above series.

The following is the case history of a patient who was given 0·6 gramme of "Mapharsen" (Parke, Davis and Company) by intravenous injection in the course of treatment for tertiary syphilis.

Case I.

The patient was a married female, aged fifty-one years. On the morning of February 17, 1947, at 9.30, she was given an injection of "Mapharsen" at a visceral syphilis

clinic. The patient states that at the beginning of the injections she felt a "vile taste" on her tongue and down her throat; the injection was completed, and after a further two or three minutes she got up and began to dress. Then she noticed gross salivation and began to feel nauseated, and she vomited green, bile-stained material with a bitter taste. At the same time the patient felt hot, began to sweat and developed "cold shivers". She was admitted to hospital at 10.30 a.m. the same day.

On her admission to hospital she was feeling nauseated and was vomiting profusely, and she began to pass many fluid stools which she was unable to control. The patient stated that she had a metallic taste in her mouth. Otherwise she did not complain of pain or other abnormal sensation. Examination on her admission to hospital revealed the patient to be a female who appeared to be about the stated age in a condition of severe prostration and great anxiety. The skin was moist and ashen grey; the pupils were dilated, but reacted to light and accommodation; the pulse rate was 110 per minute, the respirations numbered 20 per minute, the temperature was 97° F., and the blood pressure was 95 millimetres of mercury (systolic) and 50 millimetres (diastolic). She was dry retching and was incontinent of both urine and fæces. She expressed difficulty in speaking, and the speech was guttural from excessive salivation.

Apart from the above-mentioned symptoms, systemic examination showed the alimentary system to be normal. Particularly noticeable was the absence of abdominal pain and tenderness. Examination of the cardio-vascular system showed that the apex beat was in the fifth intercostal space in the nipple line; the heart sounds were audible in all areas, but were faint and distant. No accompaniments were present. The ocular fundi were normal.

Examination of the respiratory system revealed no abnormality. No abnormality of sensation or motor power was detected in the central nervous system. The superficial and deep reflexes were not altered and the cranial nerves were intact. The urine contained no abnormal constituents.

For the remainder of the day and throughout the night the patient vomited and suffered from diarrhœa. The stools contained bright blood and mucus throughout the evening, and in the morning of February 18 she was fatigued and distressed because of the severe gastro-intestinal upset. Physical examination now revealed no alteration except that the blood pressure had risen to 100 millimetres of mercury (systolic) and 90 millimetres (diastolic).

The diarrhœa ceased at noon on February 18. The patient felt more comfortable in the afternoon, and slept well that evening.

On February 19, the third day of the illness, the patient was still vomiting a little, but the vomiting had decreased to the extent that it no longer distressed her. Except for a further attack of vomiting on February 22, when she endeavoured to take solid food, the symptom was no longer disturbing.

On February 20 icterus of the sclerotics was observed, and this gradually progressed to a definite discoloration noticeable on the skin of the face, hands and abdomen. No pruritus developed; but at this stage the patient noticed that her urine was dark brown in colour. No other physical or mental abnormality was noted. The bowels were opened by enema on this day, and from then defæcation was normal, with no blood and no change in colour in the stool. The patient did not complain of epigastric discomfort and was given a light diet. No numbness or paræsthesiæ were experienced in the extremities.

On February 24 the jaundice began to grow less marked; it had completely disappeared by February 27, the tenth day of the illness. The urine was not abnormally coloured after March 1.

On February 27 the patient suffered from a mild attack of *herpes labialis*, which lasted for five days; during this time the temperature was elevated to 99·4° F. Prior to this event there had been no pyrexia.

The blood pressure rose to 125 millimetres of mercury (systolic) and 90 millimetres (diastolic) on the fourth day of the illness, and remained steady at that level.

Physical examination on March 3, prior to the patient's discharge from hospital, showed her to be a healthy woman, with no abnormal physical findings; the urine was sterile.

Examination of the urine during the period for which the patient was under observation revealed the following findings. (i) Albuminuria appeared on the third day of illness and persisted for twenty-four hours. (ii) Bile salts and bile pigments were present in the urine from February 20 to February 28. (iii) Microscopic examination on February 21 revealed that pus cells were present (0·3 cell per high-power field), occasional red blood corpuscles were present and organisms were profuse. Culture produced a moderate growth of *Bacillus coli communis*.

The hæmatological findings on February 18 are as shown in Table I.

On February 26 the bleeding time was one and a half minutes, the coagulation time was six minutes (normal control, four minutes), and the prothrombin time was 85%. (The patient's prothrombin time was 21 seconds; the control's prothrombin time was 17·8 seconds.)

The biochemical findings were as follows. The benzidine test for occult blood in fæces gave a strongly positive result on February 21, a negative result on February 26 and a negative result on March 4. On February 21 the Van den Bergh test produced an immediate direct positive reaction and an indirect positive reaction. On February 24 the serum bilirubin content was 1·9 milligrammes *per centum*, and on March 4 it was 0·3 milligramme *per centum*.

Prior to her admission to hospital at 10 a.m. on February 17, the patient received ten millilitres of 10% sodium thiosulphate solution by intravenous injection. On her admission to hospital at 10.45 on the same day the patient was treated immediately by the following measures: (i) an intravenous injection of ten millilitres of 10% sodium thiosulphate solution; (ii) gastric lavage; (iii) the passage of a Ryle's tube into the duodenum, and the administration of a 25% solution of glucose, two to four millilitres given every two hours for two days, then every four hours for a further three days; (iv) the commencement of an intravenous injection by the continuous drip method of one litre of glucose and saline solution (10%).

BAL treatment was commenced at 9.30 p.m. on the evening of February 17, and the following course was given by intramuscular injection: 4·4 millilitres *statim*, and 4·4 millilitres every four hours for three doses. Sedation was given as required, by means of potassium bromide (30 grains) and chloral hydrate (20 grains).

Routine nursing was carried out, and the patient was allowed up on March 2.

Case II.

In this case the patient was the recipient of a preparation of gold for rheumatoid arthritis. The dangers of gold administration and the precautions necessary to avoid toxic manifestations are well known, and this case

TABLE I.

Hæmoglobin Value.[1] (Grammes *per Centum*.)	Leucocytes per Cubic Millimetre.	Neutrophile Cells.	Lymphocytes.	Monocytes.	Eosinophile Cells.	Basophile Cells.
13·7 grammes = 94%	12,600	87%	13%	—	—	—
14·0 grammes = 96%	10,550	57%	30%	9	4	—
13·0 grammes = 89%	12,300	60%	33%	4	1	—

[1] 100% = 14·5 grammes *per centum*.

emphasizes the fact that individual susceptibility does occur and that complications may ensue even after the administration of small quantities of the gold preparation. "Myocrisin" (May and Baker) is sodium aurothiomalate in aqueous or oily solution, and contains 50% of gold.

The patient was a married female, aged forty-six years. During the last week of January, 1947, she began a course of "gold injections"—subsequently found to be "Myocrysin" —for rheumatoid arthritis of the hands and feet. At first she was given three weekly intramuscular injections of "Myocrisin" "single strength" (subsequently found to be 0·01 milligramme). This was followed by a period of two weeks without treatment. During this preliminary period the urine was examined every two weeks.

On about March 18 a fourth injection was given, and on the following day the patient complained of "irritation in the soles of the feet". In five days this was followed by a similar sensation in the hands. As a result of this disturbance the patient became very distressed, and she was unable to sleep at night. On March 25 a further injection was given; on the following day the irritation in the soles of the feet and in the hands became much more intense, and the patient noticed that her feet, ankles and legs were swollen; at the same time a vesicular rash appeared on the feet and hands. Despite treatment this lesion advanced and involved the face, scalp, trunk and upper and lower extremities. For some seven days prior to her admission to hospital on April 9 the patient was

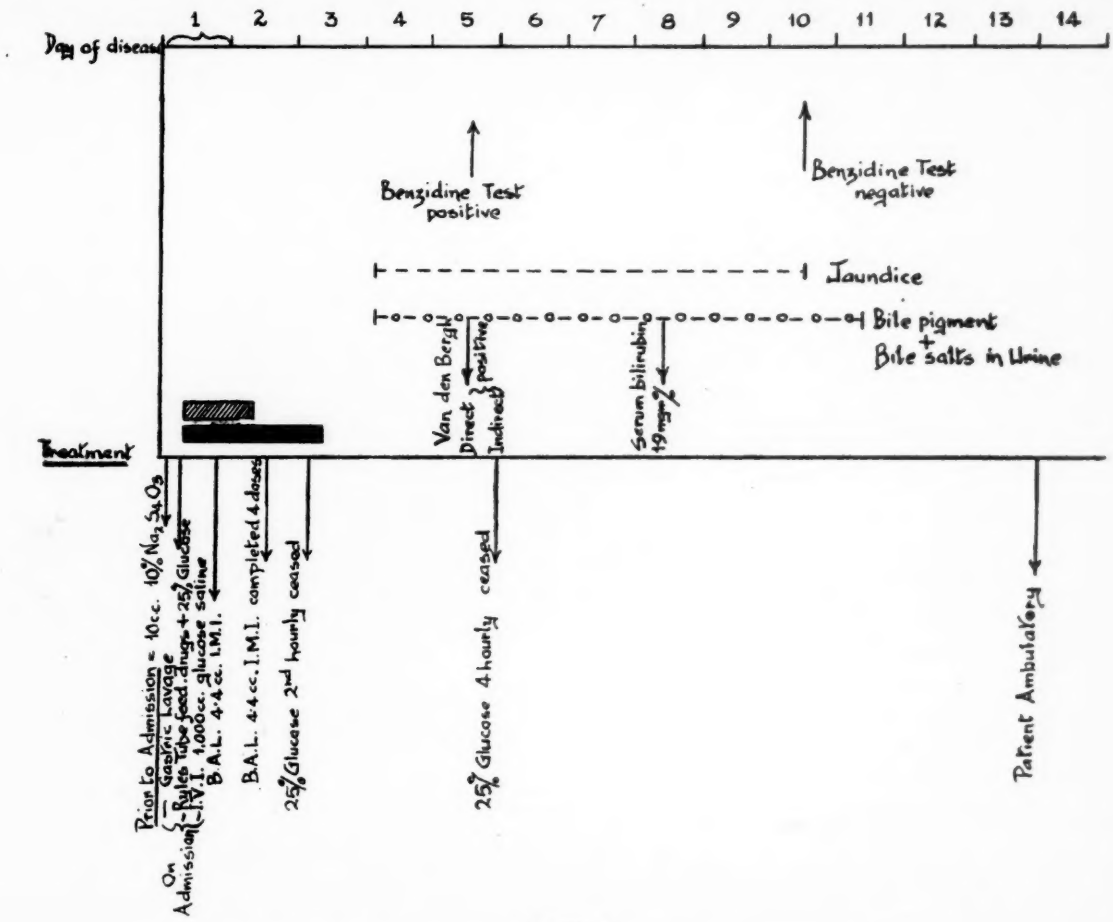

FIGURE I.
Case I. Schematic representation of treatment, findings and course of illness.

Early in March, 1947, a course of "double strength" injections (0·1 gramme) was commenced. The patient had received five of these injections at weekly intervals prior to her admission to hospital.

On careful interrogation, the patient stated that after being given the second injection of the stronger "Myocrisin", she noticed a metallic taste in her mouth, and she said that she salivated much more than usual; she volunteered the information that she was unable to appreciate the taste of food, and though she was hungry she could enjoy only drinking milk. A third injection was given, and after this she noticed that she "felt sick in the stomach" and was nauseated, though she did not vomit.

considerably distressed by the irritating sensation of her skin lesion and by her lack of desire for food. The bowels were constipated, and though she was nauseated, the patient had vomited on one occasion only—the night of April 4. She complained of no abdominal pain or discomfort on her admission to hospital, but the dryness of her mouth, together with a metallic taste, caused her much concern. The patient stated that, though she had difficulty in passing her urine and it was diminished in amount, she had noticed no alteration in its colour nor any odour from it.

Specific interrogation revealed no symptoms referable to the other systems. The previous health and family history were not relevant.

On examination, the patient was seen to be a woman of about the stated age; she was anxious and in obvious discomfort. Inspection of the skin revealed the presence of severe widespread acute exfoliative dermatitis affecting the scalp, jaw, neck, trunk and upper and lower extremities; these lesions were in varying stages of development, from large vesicles containing a turbid serous fluid exudate to large encrusted areas. The lesions were more advanced and severe about the ankles and feet and also the wrists and hands; the face was extensively involved, and a mild degree of ocular conjunctivitis was present. Movement of the body or limbs in any direction caused the patient severe distress, and consequently examination and investigation were reduced to a minimum. Examination of specific systems revealed no abnormality in the cardio-vascular system. The blood pressure was 130 millimetres of mercury (systolic) and 90 millimetres (diastolic). The pulse rate was 84 per minute; no abnormal findings were observed in the heart. No abnormality was detected in the central nervous system, the respiratory system and urinary system. Abdominal examination revealed a mild degree of epigastric tenderness, otherwise no abnormal physical signs were present; the mouth and tongue were dry, but no evidence of oral or gingival ulceration was noticed. The patient weighed 105 pounds on her admission to hospital, and her temperature was 99° F.

Laboratory investigations at that time gave the following results. No abnormality was detected in the urine on chemical or on microscopic examination. The blood urea content was 72 milligrammes per 100 millilitres. The protein content of the blood serum was 5·3 grammes per 100 millilitres. A full blood count gave the following information: the erythrocytes numbered 4,650,000 per cubic millimetre, the hæmoglobin value was 11·6 grammes *per centum* (79%; 100% is 14·5 grammes), and the hæmatocrit reading was 40% of packed red cells; the leucocytes numbered 10,500 per cubic millimetre, 61% being neutrophile cells, 19% lymphocytes, 9% monocytes, 10% eosinophile cells and 1% basophile cells. Macroscopic examination of the fæces revealed a well-formed stool, pale in colour; the benzidine test for occult blood produced a negative result.

Treatment was commenced on the patient's admission to hospital on April 9, and was as follows. One ampoule (2·2 millilitres) of BAL was given by intramuscular injection for four doses. Penicillin (15,000 units every three hours) was given by intramuscular injection. A preparation of zinc cream was ordered for local application to the skin lesions. Fluids were given by mouth, and a diet rich in protein was ordered. On April 10 the BAL dosage was increased to 4·4 millilitres every six hours for four doses, followed by 4·4 millilitres twice a day for two days. (The small initial dose of BAL was necessary pending availability of a further supply of the drug. The penicillin was given as a prophylactic measure, in view of the widespread nature and severity of the lesions.)

On the second day of her stay in hospital (April 11) the patient said that the irritation in the lesion was much less intense; she was much brighter, appreciating her food, and her condition generally was better. The skin lesions were much relieved, and the affected areas were dry and the erythema was noticeably less; no fresh vesicles were seen. No abnormality was detected in the urine and fæces, and physical examination of the body systems revealed no essential changes from those previously recorded. The temperature was normal. On April 12 a full blood count gave the following results: the hæmoglobin value was 12·6 grammes *per centum* (87%); the leucocytes numbered 13,100 per cubic millimetre, 55% being neutrophile cells, 23% lymphocytes, 4% monocytes and 18% eosinophile cells. The patient continued to progress, and on April 15 the skin surface was clean and no lesions were seen. On April 20 she was allowed up, and examination of her blood and urine revealed the following findings. No abnormality was detected in the urine on chemical or microscopic examination. No bilirubin was detected in the blood serum. A full blood count gave the following information: the hæmoglobin value was 14·0 grammes *per centum* (96% of normal); the leucocytes numbered 8,500 per cubic millimetre, 48% being neutrophile cells, 23% lymphocytes, 7% monocytes, 21% eosinophile cells and 1% basophile cells. The blood sedimentation rate was ten millimetres in one hour.

Discussion.

In Case I the patient was known to have had syphilis, and had been treated for syphilitic meningitis since 1936 with routine antiluetic therapy. On this occasion she received 0·6 gramme of "Mapharsen" intravenously. This is ten times the standard doseage (0·06 gramme) used in recognized courses of anti-syphilitic therapy. The arsenic content of "Mapharsen" (Parke, Davis and Company) is 31% of trivalent arsenic, and so this patient would have received 2·87 grains of that metal intravenously. The minimal lethal dose of arsenic is usually given as two grains. A case of death from "Mapharsen" injection is reported,[1] in which the patient received 0·6 gramme of the material.

Therapeutic measures other than BAL were used because this substance was unavailable and had to be flown from Victoria; in view of the gravity of the situation and of the inevitable delay, the standard line of treatment was adopted. However, the short duration of the immediate toxic effects and the very short course of the illness, with complete absence of such complications as encephalitis, exfoliative dermatitis, peripheral neuritis *et cetera*, may with some justification be accredited to the efficacy of BAL in the treatment of this patient.

In Case II the value of BAL in the rapid recovery of the patient was striking. Particularly noticeable was the short convalescence of this patient, for in the space of eleven days an acutely ill patient with extensive acute exfoliative dermatitis was relieved of her skin lesions and was able to leave her bed.

The importance of BAL as an adjunct to therapy in cases of gold intoxication will be of great interest in the future, for although references are made to its use in such cases in the various reports, only one fully published account of its clinical use in gold intoxication is available.[2]

The substance BAL (British Anti-Lewisite OX217, −2.3 dimercaptopropanol−($CH_2SHCH_2SHCH_2OH$) was evolved during the recent war, and until recently has been on the secret list. It is a penetrant oil and is 6% soluble in water. It is a specific antidote for systemic arsenical poisoning, and its administration is recommended in all cases of such poisoning, whether in the early or late stages. Thus it has a definite place as an antivesicant for skin lesions, in eye degeneration, and in complications of systemic arsenical poisoning such as dermatitis and encephalitis. Work is progressing in an endeavour to determine the benefit of this substance in other heavy metal intoxications, and the result on the effects of mercuric chloride and nickel poisoning is encouraging.

It has been shown that BAL is highly effective in stopping the toxic action of Lewisite upon the tissue oxidase system, and in addition it can reverse this effect should it became established. As a consequence this therapeutic agent can be successfully used some time after the dose of arsenic has been administered.

The vehicle is a 10% solution of benzyl benzoate in arachis oil, in which BAL is incorporated to form a 10% solution.

The dosage according to body weight is as follows: 2·5 millilitres if the weight is 125 pounds, 3·0 millilitres if the weight is 150 pounds, 3·5 millilitres if the weight is 175 pounds, 4·0 millilitres if the weight is 200 pounds; the solution is given *statim* by intramuscular injection.

The initial dosage is repeated every four hours for four doses in ordinary cases. If poisoning is severe, the second injection is given after two hours and then single half-doses are given each day for three to four days.

Side effects of the drug do occur, but they are reported not to be sufficiently severe to contraindicate a course of four injections. Among the effects which have been described are a feeling of constriction of the throat, oppression of the chest, burning of the lips, reddening and lachrymation of the eyes, dryness of the mouth, nervousness and restlessness, nausea, vomiting, local tenderness

and a transient rise in blood pressure. These side effects may be relieved by the use of barbiturates.

Acknowledgements.

I wish to express my appreciation to Professor C. G. Lambie and Dr. T. M. Greenaway, under whose care these patients were admitted to hospital, for permission to report these cases. Also, I wish to thank the members of the medical and nursing staff of the Royal Prince Alfred Hospital for their assistance.

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PENETRATING GUNSHOT WOUND OF A PREGNANT UTERUS.[1]

By R. J. DE N. SOUTER,
Yankalilla, South Australia.

J.H., a single girl, aged twenty-one years, accidentally shot herself in the abdomen at about noon on November 20, 1946. She was first attended at the site of the accident, when she was found to be in great pain and sweating freely, and to have a rapid pulse. She was given one-quarter of a grain of morphine and carefully removed to hospital. A laparotomy was performed, and the patient was found to be over seven months pregnant. The missile, a 0·22 rifle bullet, had charred the clothing in the right loin and entered the abdominal wall between the last rib and the ilium; it had emerged three inches below and to the left of the umbilicus. The only viscus damaged was the uterus, which had two holes in the anterior wall five inches apart, the entrance wound being the larger. A quantity of blood clot in the abdomen was removed, and hæmorrhage from the uterus was controlled by oversewing the wounds. The parietal wounds were excised and the abdominal wall was closed.

No complications occurred, except that on November 25 an uneventful labour took place and a female baby weighing five and a half pounds was born. It was found that the child had been shot through the right thigh, half-way between the hip and the knee. These wounds were sutured; but after a week they broke down and healed by secondary union. In February, 1947, the baby was thriving, though she had not been due until January 12. She was being breast fed by the mother, who also had suffered no ill effects.

[1] This case was discussed at a meeting of the South Australian Branch of the British Medical Association at the Royal Adelaide Hospital on February 21, 1947.

Reviews.

A TEXTBOOK OF MIDWIFERY.

IN the second edition of his "Textbook of Midwifery", as in the first, Wilfred Shaw approaches the problems of treatment from the angle of the principles involved.[2] He emphasizes the need for great clinical judgement in the accoucheur, and of operative skill and dexterity of a very high order. New material has been added on many subjects such as the rhesus factor, *erythroblastosis fœtalis*, chemotherapy, including penicillin and the sulphonamide drugs. In regard to the Rh factor, the author, after describing the treatment to be adopted for the infant, points out that recovery is not always possible on account of degenerative changes in the basal ganglia and the nerve tissues in general, and that of those infants who do recover a certain proportion are afflicted by spastic pareses. The author deprecates the tendency to hold too rigidly to any form of routine treatment for obstetric emergencies: in discussing Cæsarean section in eclampsia, he regards it as having a definite place in the treatment in fulminating cases; in dealing with episiotomy, he states, "the greater the skill of the obstetrician, the less frequently does he perform the operation". He warns against the dangers of meddlesome midwifery, and emphasizes the fact that parturition is the application of mechanics to a vitalistic process; he gives clearly his reasons for the belief that not all the disasters of parturition are preventible, and points out the folly of infatuation with the maternal mortality rate. Some useful advice is given from the practical viewpoint of the distribution of difficult cases, in the organization of domiciliary and hospital attention for patients with conditions which are regarded as abnormal or likely to be. In his discussion of intranatal death of the fœtus we should have preferred the author to emphasize the importance of prolonged labour as a factor in causing asphyxia. The book is concisely written, well set up and printed, while brevity and clarity are outstanding features.

[2] "Textbook of Midwifery", by Wilfred Shaw, M.A., M.D., (Cantab.), F.R.C.S. (England), F.R.C.O.G.; Second Edition; 1947. London: J. and A. Churchill, Limited. 8½" × 5½", pp. 664, with many illustrations. Price: 21s.

A YEAR BOOK OF SURGERY.

"THE 1946 YEAR BOOK OF GENERAL SURGERY", like many of its predecessors, has been edited by Dr. Evarts A. Graham.[1] It is, as most practitioners know, a member of the "Practical Medicine Series" of year books, the series being thirteen in number. Volumes of this kind are most useful to the busy practitioner who can without too much effort gain a bird's-eye view of recent work.

This year's volume on surgery starts with a section on anæsthesia and analgesia. This has five subdivisions, dealing respectively with inhalation anæsthesia, combined anæsthesia, intravenous anæsthesia, intrasternal anæsthesia and spinal anæsthesia. Reference is made to the use of curare with nitrous oxide for lengthy operations. The editor commends the procedure described, but at the same time he draws attention to an article setting out the dangers of nitrous oxide. A special apparatus for the combined use of curare and "Pentothal" is described. The intrasternal anæsthesia described comprised the intrasternal administration of "Pentothal" to a Japanese prisoner after several unsuccessful attempts at venepuncture.

In the section on asepsis and antisepsis short reference is made to streptomycin in the treatment of surgical infections. Streptomycin sterilizes the blood stream provided the infecting organisms are susceptible to a safe serum concentration of the drug. It is stated to be valuable in septicæmia due to *Escherichia coli, Aerobacter aerogenes, Pseudomonas aeruginosa* and other Gram-negative bacilli.

The section on operative technique contains reference to investigations by Correll and his co-workers on a new absorbable gelatin sponge.

After a small section on wound healing and another on tumours there is a section on blood vessels. This includes references to procedures that would have been thought impossible a year or two ago. Thus we read of the technique of immediate restoration of vascular continuity after arterial wounds, the surgical management of acute arterial occlusion, the ligation of the inferior *vena cava* and iliac veins, operations for *ductus arteriosus*, the establishment of portacaval shunts for portal hypertension and the surgical correction of coarctation of the aorta.

The treatment of acute and chronic osteomyelitis with penicillin is described in the section on bones. The section on fractures is short and deals with general principles, and sections on scalp and skull, brain and meninges, face and mouth, neck, thyreoid and mamma follow. In the section on the brain attention is drawn to an important paper by Fincher, who used craniotomy and total dissection in the treatment of brain abscess.

Surgery of the chest is dealt with in a small section. Abscess of the lung is considered and a method for the closure of the bronchus in pneumonectomy and lobectomy is described. Reference is made to a case of multiple pulmonary hæmangiomata, 38 cases of adenoma of the bronchus

[1] "The 1946 Year Book of General Surgery", edited by Evarts A. Graham, A.B., M.D.; 1947. Chicago: The Year Book Publishers, Incorporated. 7" × 4½", pp. 680, with illustrations. Price: $3.75.

are mentioned, and surgery of the thymus gland is discussed, reference being made to the report by Geoffrey Keynes in which he deals with 51 thymectomies for *myasthenia gravis*. In the section on pulmonary tuberculosis the work of Robb, of Auckland, on the resection of pulmonary tissue in tuberculosis is mentioned.

An interesting discussion reminiscent of Ochsner and Sherren comes from the pen of George Crile, junior, and J. R. Fulton. They base their conclusions on 1,500 appendicectomies and point out that in the first twenty-four hours surgery is the ideal treatment for acute appendicitis. In the next twenty-four hours complications are apt to occur more frequently than at other times. Up to forty-eight hours it is possible to remove the appendix without rupturing an abscess. After forty-eight hours the attack is subsiding without complications or sometimes a localized peritonitis or walled-off abscess has developed. At this stage the two authors think that it is questionable whether surgical intervention is of value. The editor remarks that these observations and conclusions will not be accepted without challenge. What is termed an improved method of extraperitoneal closure of a colostomy stoma has been described by Shallow, Eger and Tourish. Special attention is drawn by the editor to work by Curtis and Movitz on the surgical significance of accessory spleens. The presence of these bodies may offer an explanation for failure to achieve a satisfactory result after splenectomy for hæmolytic jaundice and thrombocytopenic purpura.

The section on the spine and spinal cord contains worthwhile references to pilonidal cysts and their operative treatment. Two sections, on the upper and lower extremities, bring this useful volume to a close. There is a satisfactory index.

JAUNDICE.

"THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE", by L. Schiff,[1] is a book of 313 pages and represents an attempt by the author to produce a treatise containing "a discussion of the chemical and pathological features of the disorders accompanying the icterus, a description of the laboratory techniques used . . . and an interpretation of the results obtained by these methods of study". This is set out in the preface with comments on the present position of homologous serum jaundice. The importance of the diagnosis of neoplastic from parenchymal jaundice is stressed in the same section. The introduction adequately describes the characteristics and classifications of jaundice. Following this are 187 pages dealing with the various conditions in which jaundice occurs. These are short and concise descriptions, but we doubt if there is anything here that has not already been written in the sections on diseases of the digestive system in textbooks of medicine. As this comprises almost two-thirds of the whole, the impression remains that the title of the book is a misnomer, and that it might have been better called "Conditions Causing Jaundice".

The book ends with a section on chemical and laboratory aids in the differential diagnosis of jaundice and an appendix actually describing the laboratory methods. We feel that this is defective as a critical appraisal. This section includes fourteen radiographs and ten photomicrographs of liver biopsy specimens, all of which are excellent.

Though this book contains a concise description of the diseases connected with jaundice, it adds little to the information available in textbooks of general medicine.

INFECTIOUS DISEASES.

FOUR years ago, when the second edition of "Clinical Practice in Infectious Diseases"[2] appeared, the authors made apologies for the delay in its publication, caused by difficulties which could not be avoided in the England of wartime. That edition was sold out in a few months, and was never reprinted, for the printing works and the whole of the blocks were destroyed by fire. The authors wisely decided to rewrite and to enlarge the book, and to face boldly the same difficulties all over again. It may be remembered that the second edition contained a hundred pages of additional matter; the enlargement is even greater in this new volume, and it is so thoroughly dispersed that hardly a single page of the original work remains in its entirety.

The general form of the second edition has been kept, but the pneumonias have been grouped into a separate chapter, in which primary atypical pneumonia is discussed more fully. The most notable of such wider discussions is contained in Chapter XXXV, which comprises the first part of the section dealing with management of infectious diseases, and describes the use of the sulphonamides and penicillin. Nearly fifty pages are devoted to this subject. The sub-chapter on the sulphonamides in the preceding edition was regarded by many as a model exposition, and equal praise will be accorded to that on penicillin, which is given similar full treatment, in contrast with the modest note contained in the earlier edition.

To the chapter on infective enteritis has been added an account of recent work on the nature of dehydration and its influence on the management of this condition in children. Much more information is presented on old and new subjects, by either brief mention or detailed description. Some of the more important comments are those on airborne infection, ventilation and aerosols, homologous serum jaundice, plasma proteins, the present and prospective use of γ globulin, and phage typing of typhoid and paratyphoid organisms. The matter of the book is so highly condensed that here and there are short passages which are difficult to read, but generally the authors have maintained the clarity of expression which characterized their original work. Little or nothing in recent relevant literature has escaped them; the book is now a work of reference for practitioners of all classes, and retains its position as the best in the language on the subject.

PHYSIOLOGICAL CHEMISTRY.

FROM 1907 to 1947, "Practical Physiological Chemistry", by P. B. Hawk and various collaborators, has been in the front rank of reliable laboratory manuals and source books of information on experimental biochemistry. The publication of the twelfth edition this year, ten years after the eleventh edition, is an important event for all biochemists, physiologists, pathologists and students of nutrition.[1] It fully maintains the high standard set by the earlier editions.

This new edition contains 350 more pages than the previous one and the whole of the book appears to have been revised. Little seems to have escaped attention and some sections introduced into this book form agreeable surprises. There are new sections on the principles and practice of photometric analysis, the electrophoretic separation of plasma proteins, the composition of foods, the newer vitamins, the clinical significance of vitamins, isotopes in medicine, the polarograph, the "sulpha" drugs, antibiotics and metabolic antagonists and manometric technique. This list of new sections indicates the wide scope of the contents. The section on nutrition includes a good account of the techniques of microbiological assay.

In no other book will there be found such an up-to-date selection of modern techniques accurately described and fully annotated with the necessary references and relevant general information. As far as we can judge, the selection of methods is admirable and, generally, alternative methods are described. We can find no fault with the new edition. This book has always included in each section a preliminary concise statement of the facts and principles involved. Not everyone will approve the extent to which this practice has been carried out in the now large volume. This edition containing 1,323 pages can be regarded as a textbook of both the theory and the practice of physiological chemistry. We consider it a unique volume which should be purchased for all laboratories concerned with biochemical procedures, routine or research. It should be accessible to all technicians in hospital and biological laboratories. Not that we mean that it is another large manual for the use of hospital laboratory workers; it contains the requirements for a very good undergraduate course.

The setting out and printing are very pleasing and efficient for use. The indexing is good. The special binding material and cover, selected for wearing quality in laboratory handling, complete a very useful and highly authoritative volume.

[1] "The Differential Diagnosis of Jaundice", by Leon Schiff, Ph.D., M.D.; 1946. Chicago: The Year Book Publishers, Incorporated. 8" × 5¼", pp. 320, with illustrations. Price: $5.50.

[2] "Clinical Practice in Infectious Diseases: For Students, Practitioners and Medical Officers", by E. H. R. Harries, M.D. (London), F.R.C.P., and M. Mitman, M.D. (London), F.R.C.P., with a foreword by Sir Allen Daley, M.D. (London), F.R.C.P.; Third Edition; 1947. Edinburgh: E. and S. Livingstone, Limited. 8½" × 5½", pp. 690, with illustrations. Price: 22s. 6d.

[1] "Practical Physiological Chemistry", by Philip B. Hawk, Ph.D., Bernard L. Oser, Ph.D., and William H. Summerson, Ph.D.; Twelfth Edition; 1947. Philadelphia, Toronto. The Blakiston Company. 9" × 6", pp. 1,336, with illustrations. Price: $10.00.

The Medical Journal of Australia

SATURDAY, JULY 26, 1947.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

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PREVENTIVE MEDICINE AND THE FUTURE OF MEDICAL PRACTICE.

BERNARD SHAW, with his remarkable capacity to make penetrating and half-true statements, says in the preface to "The Doctor's Dilemma": "Doctoring is not even the art of keeping people in health: it is the art of curing illnesses." And again: "The healthier the world becomes, the more they [the medical practitioners] are compelled to live by imposture and the less by that really helpful activity of which all doctors get enough to preserve them from utter corruption." On the other hand it has become commonplace in medical circles to say that the ultimate goal of medical practice is replacement of clinical and therapeutic medicine by preventive medicine, and that the more enlightened section of the medical profession (which surely includes the great majority, Mr. Shaw notwithstanding) is striving towards professional suicide. These latter statements are highly significant and far-reaching in their implications, and when such statements come to be commonplace, it is usually time for them to be reexamined. It is much too easy to take a generalization for granted and to leave its implications unexplored. For this reason most members of the profession will share the feelings of Perrin H. Long[1] when he says that he was amazed, on reading the report on the United States medical curriculum, prepared by the Association of Medical Students and Interns from the returns of a widely disseminated *questionnaire*, to find that instruction in public health (preventive medicine) stood third in the list of subjects which, in the opinion of the respondents, should be de-emphasized. Professor Long, who is from the Department of Preventive Medicine of the Johns Hopkins University School of Medicine, and is recording an address given to a conference of professors of preventive medicine, remarks that the report should not be lightly dismissed; and such an expression of opinion from a large number whose practical influence is yet to be felt, running counter as it does to accepted trends, must provoke general thought. Long goes on to discuss just what is meant in current thought by preventive medicine and finds great diversity of opinion and definition. He quotes with approval Ryle's finding that "three great historical epochs exist in preventive medicine". During the first epoch the initial approaches to sanitation, proper working conditions, adequate housing *et cetera* were made, and empirical methods for control of many infectious diseases were put into effect. These measures were continued and extended in the second epoch under the influence of the development of microbiology and sanitary science to a point which, at least in certain parts of the world, has brought many infectious diseases under control and reduced their ravages to a minimum. At present, Long remarks, we are living in the end of the second and in the beginning of a third epoch, in which prominence will be given to the prevention of non-infective diseases, the rehabilitation of the sick, and the mitigation of chronic or degenerative disease. An exact definition of preventive medicine is difficult to find, and many writers are quoted with varying conceptions of the subject. Most, however, are convinced of the importance of a clinical approach to its teaching and practice. Long emphasizes his view that preventive medicine is "not public health in the general educational or practical sense"; it is not tropical medicine nor industrial medicine; and it is not a speciality in the ordinary sense. "Preventive medicine is a philosophy, a way of thought and life, a subject which should permeate a large part of the medical curriculum and the whole of the practice of medicine." This is really a splendid conception, and, for all that it sounds like a string of abstract phrases, it is essentially a practical conception, which gives the subject its true relation to medical practice.

Long then discusses at some length the clinical approach to the subject especially in relation to its teaching. He quotes Smillie as pointing out that the mission of undergraduate instruction in preventive medicine is not "to prepare students to become grade-B health officers", but rather "to meet their obligations as private practitioners of medicine". Similarly clinical teaching is inadequate if the interest of the student is "focused on the sick man recumbent on a hospital bed" with little or no attention paid to what brought him there or what happens before he is fully rehabilitated. Competing with the "vast quantities of precise and intricate information" which students are expected to assimilate, preventive medicine as a separate "special" subject is liable to be overshadowed or seen from a distorted angle. Its true place is as part of clinical medicine. Long, speaking essentially as a teacher of his subject to other teachers in conference, discusses the practical aspects of bringing preventive medicine more closely into the medical curriculum; but it is not perhaps opportune to comment on these details beyond drawing attention to the aim which Long suggests for a department of preventive medicine: "One of gradual self-extinction in every medical school." "Its success should only be considered complete when, owing to its efforts and endeavours, the level of the instruction in and practice of humanistic medicine has been raised to such a point in all departments in a medical school that the continued presence of a department of preventive medicine is unnecessary."

[1] *The Lancet*, April 5, 1947.

But what of the doctor in practice? Is he soon to abolish his own practice by encouraging the introduction of preventive measures against disease? This is a Utopian possibility which need not concern our generation at least. But it still remains for the profession as a body as well as for the individual practitioner to realize that preventive medicine is far more than good sanitation and successful inoculation campaigns. The promotion of health in a positive way and the complete rehabilitation bodily and mentally of those who have been sick and have "ceased treatment" are community matters, and the present trend is for the community to assume such responsibilities. Apart from his personal contact with the individual patient, the medical practitioner has a responsibility as a citizen in these things and a special responsibility as a specially informed citizen. In the country town he is still "the doctor" whose exact scientific knowledge is only part (and perhaps not the most important part) of the equipment which fits him in the public eye to express an opinion and wield influence on many matters. It is not wise that this responsibility should be under-estimated—nor the scope of the task, for the task would certainly not be fulfilled by the creation of a race of physically perfect beings who were stunted and degenerate in their intellectual and moral outlook and stillborn in things of culture and things of the spirit. The great majority of the profession, both in town and country districts, will undertake this task willingly and look to its fulfilment as far as it lies within the power of man, despite Mr. Shaw's assertion that "of all the anti-social vested interests the worst is the vested interest in ill-health".

Current Comment.

RICKETTSIALPOX: A NEWLY RECOGNIZED DISEASE.

A PREVIOUSLY unclassified disease has been described in America, and, in view of its significance in differential diagnosis, brief reference to it seems desirable, though there is no indication that it has occurred or will occur in this country. Morris Greenberg, Ottavio Pellitteri, Irving F. Klein and Robert J. Huebner have published an account of their observations on 144 affected subjects.[1] The disease, to which the rather ungainly name "rickettsialpox" has been given, is considered to be due to a rickettsial organism, *Rickettsia akari*, which has been isolated from the blood of affected patients and also from certain rodent mites, *Allodermanyssus sanguineus*. The principal clinical features were as follows. In the first place the initial lesion commenced as a papule, proceeding to form a deep-seated vesicle, and finally a black eschar. It was seen chiefly, but not exclusively, on the covered parts of the body. The regional lymph glands were usually enlarged. The lesion persisted approximately for three weeks and usually left a small scar; its occurrence was sometimes denied, but it could generally be demonstrated on careful inspection. Secondly, the onset was sudden and was characterized by chills, fever, sweats, backache and lassitude. It usually occurred about a week after the beginning of the initial lesion. The fever lasted from two to ten days. Headache, mostly frontal, was common and severe. Most patients did not appear acutely ill and none died. In the third place the rash was characteristic and occurred in all cases. It appeared early (within four days of the onset of fever in most cases) and lasted, on the average, four to seven days. The lesions were at first maculopapular, discrete and erythematous; in a day or two a vesicle developed on the summit of the papule, and finally dried, to leave a dry crust which fell off without scar formation. There was no pattern in the distribution of the rash; in two instances lesions were seen in the mouth. There was no accompanying itching or pain. The usual bacterial agglutination tests gave uniformly negative results; however, antibodies for the disease could be demonstrated by means of the complement-fixation test.

Recognition of this disease as a clinical and pathological entity is important in the differential diagnosis of a number of other diseases. Earlier cases were confused with chickenpox, but rickettsialpox differs in the deeper, firmer character of the vesicles, the initial lesion, and the complement-fixation reaction. In the case of smallpox, the pock, though similar in its earlier stages, becomes pustular and heals to leave a scar; the rash has a characteristic centrifugal distribution; no initial lesion is found and the illness is much more severe; serological tests will ultimately differentiate the two. Infectious mononucleosis has a characteristic blood picture. Typhus (epidemic or endemic) differs in the type of rash and its serological reactions. Scrub typhus, in which the initial lesion may be a cause of confusion, differs completely in the nature of the rash and usually manifests serum agglutination with Proteus OX K. Rocky Mountain spotted fever and boutonneuse fever are also mentioned for completeness. There are no grounds to suspect that rickettsialpox is among us, but in view of the confusion in diagnosis which its appearance in New York caused among medical practitioners in that city, it seems as well to know about it.

[1] *The Journal of the American Medical Association*, March 29, 1947.

PHTHIOIC ACID.

AMONGST the many interesting subjects discussed by Sir Robert Robinson in his presidential address to the Royal Society of London[1] there was one which, though centred on a highly technical research in a most difficult branch of organic chemistry, must be regarded by the medical profession as possessing considerable importance. This investigation was carried out by Sir Robert Robinson in his laboratory with the collaboration of Dr. Coulthard, of Boots Pure Drug Company, Limited, and Dr. Ungar, of Glaxo Laboratories, Limited. It is interesting to note *en passant* that commercial concerns are now able and willing to attract and to keep men of science of high standing not only on the commercial side, but in what might be termed academic theory. The tubercle bacillus, as is well known, possesses a waxy envelope which confers some powers of resistance to therapeutic agents. The suggestion that the true anti-tuberculosis drug should be fat-soluble, so that it could pass through this protective envelope, turned out to be not so sound as was expected, for this very fat-solubility leads to the drug being accumulated in the capsule of the bacillus just as a generation ago carbolic oil was found to be worthless as an antiseptic as the phenol clung to the oil and was partitioned only in minute amount to the water-soluble constituents of the invading germ. The next step was to find a compound chemical which contained a fat-soluble moiety linked to a water-soluble moiety, which latter would be the active sterilizing agent and which would be bound to the fat-soluble part by a readily hydrolyzable linkage. This is the basis of considerable research now in active process of investigation. Whatever the outcome of this particular quest may be, it is obvious that the chemical nature of the limiting membrane of the tubercle bacillus would soon be subjected to analyses by highly expert organic chemists. One ingredient of this envelope was soon discovered to be methyl stearic acid and was named tuberculo-stearic acid. Another component was shown to be an acid, $C_{29}H_{52}O_2$, and was named phthioic acid, the constitutional formula of which is a straight chain of 23 carbon atoms with three methyl branches. The special significance of phthioic acid is that it produces, when injected into susceptible animals, lesions identical

[1] *Proceedings of the Royal Society*, Series B, No. 875, Volume CXXXIV, March 25, 1947.

with those arising from tuberculosis invasion. Soon the organic chemist got busy and a number of branched, long-chain fatty acids with a methyl group in the 3 position was obtained, all with similar toxic powers. This research is still in its infancy and dramatic results may be expected.

As is usually the case, totally unrelated researches began to present converging evidence. It was found that when cholesterol is given to rats there is a breaking up of the complex molecule at the places where each of the four rings is fused with its neighbour and a branched long-chain fatty acid is produced with a methyl group, though without apparent toxic attributes. Whether this remarkable disintegration of a fairly stable tetracyclic compound is carried out in the rat's tissues or by the bacteria of the alimentary canal, we are not told. Another suggestive piece of work is that the long chain of oleic acid can curl round and the two ends be united like the Aztec symbolic snake with its tail in its mouth, thus producing civetone, the odoriferous principle of the civet cat; similarly muscone, the very similar principle of the musk rat, was found to be 3 methyl palmitic acid with terminals united, and conjectures as regards possible relations with phthioic acid have been aroused. There are also indications that the pathological role of phthioic acid may not be confined to tuberculosis, for what looks like tuberculous tissue has been found by several investigators to be associated with certain tumours.

The possible outcome of these researches is either to prepare a drug which will make a frontal attack on the tubercle bacillus, or, what seems more likely, to apply the abnormal lipins to the development in the human body of effective immunization.

INTELLIGENCE AS A SOCIAL PROBLEM.

IT might seem paradoxical that in studying and applying tests of intelligence to individuals there may be a danger of producing difficulties which could seriously interfere with the balanced development of society. This problem is considered in the twentieth Maudsley Lecture, delivered by F. C. Bartlett, Professor of Psychology in the University of Cambridge.[1] He comments on the extraordinary zeal shown in devising and applying tests designed to measure intelligence. One result of this activity has been the modification or even abandonment of the earlier ideas about intelligence, for, while accepted tests are realized to be of value, it is not always clear what it is that they are applied to reveal. From being a fixed single quality, intelligence has come to appear as a very complex function with a considerable number of factors. But if we leave academic arguments about this on one side for the moment, it seems safe to admit that it is one of the characteristics of an intelligent person to deal fluently with those symbolic forms which exteriorize certain phases of thought, and which form the basis of most of our educational training. At least, says Bartlett, this view has been defended by first-class thinkers, though experience is now indicating certain risks to a society which accepts it without reservation. The author first began to be seriously disturbed about the validity of this assumption during the war, as the result of his observations on the results of intelligence tests used in the selection of pilots for the Royal Air Force and controllers of operation rooms directing air manœuvres. There was no doubt that a fairly high level of intelligence was needed for each of these activities; high scoring in the tests enabled a confident forecast of mental fitness for the task to be made, and *vice versa*. But there were substantial exceptions at both ends of the scale which were not easy to explain. The question was whether the intelligence that deals with symbols might not be radically different from that which deals with situations as such. The results of tests for dark adaptation also raised points of interest. These tests involved recognition of realistic forms, thus being in part a measure of what the author calls perceptual efficiency, which might seem to have some intellectual basis. Yet the scores in the tests did not accord with the intelligence ranking with any constancy. Further experiment proved that the recognition of objects seen from an unusual angle, as in aerial photography, and the speed and accuracy with which readings of grouped dials could be made, had no necessary relation to intelligence. Preliminary experiments on the testing of manipulative efficiency gave similar results, though levels of efficiency in perceptual and manipulative capacity are apparently not related. Bartlett here points out how important it is that further knowledge should be gained on these subjects, for if it is true that these qualities, obviously most useful in the social groups of civilized communities, are not regularly related to "intelligence" as the term has been accepted in a pragmatic sense, there may be risk in the large-scale employment of intelligence tests. Another interesting observation was made on the comparison of the war-time intelligence tests with the record of the pre-war occupation of the individuals concerned. Scrutiny of ten thousand records showed that the majority of citizens appeared to be adaptable to most of the usual occupations, taking continuous employment as evidence of reasonable suitability. The only striking differences appeared at the extremes of the range. It is of course known that most of the intelligence tests produce "bunching" in the upper range, which seems to show that the tests become less discriminative at these levels. Another difficulty in assessing an individual's absolute capacity, apart from comparative tests, is that little is known of the variations in the capacity to improve scoring in a test by practice or repetition. The summation of these observations is that the approved tests of intelligence, by reason of their preoccupation with symbolic efficiency, may fail to give due recognition to certain forms of skill whose significance and value to a mechanized community are rising rapidly.

The author points out further problems for students of social relations. By the use of present methods it would appear that about one in five of the total school population of Britain has an intelligence level sufficient to guarantee success in university examinations. This figure is believed to have increased considerably from earlier standards. If the time comes when the whole school population, with the exception of the mentally defective, is found to fall into this category, what then? Post-graduate studies at Cambridge show that the preferences of individuals and groups for certain vocations bear no balanced proportion to the demands of society. Perhaps the time approaches when the majority of people will have to try to satisfy themselves in an occupation relatively low in their private priority of desire. On the one hand we are building up a scale of social values heavily weighted in very restricted directions, and on the other hand our civilization is becoming more and more heavily industrialized. Some of these problems take us far beyond the scope of individual tests of capacity and suitability of intellect, but there is a danger that we may actually increase disappointment and frustration, of which all men and women have already had enough. It is by no means impossible to imagine a time when everyone will carry through life's journey his intelligence index, which would largely determine his status and duties in society. This, as the author points out, may be regarded as the dream of a visionary or a nightmare, according to our views. There is need for more work on all aspects of these subjects, for they are intimately related to the responsibility of man with regard to the destiny of his race.

[1] *The Journal of Mental Science*, January, 1947.

"Q" FEVER IN THE UNITED STATES.

E. H. DERRICK, of Brisbane, in 1937 described a new fever-entity which he provisionally named "'Q' fever". Investigations revealed the occurrence of cases of the disease since 1933. Culled from the composite group of conditions known in Queensland as "coastal fever", "Q" fever had characteristic clinical features and mostly occurred among meat workers and dairy farmers. From material supplied by Derrick, F. M. Burnet, of Melbourne, isolated a rickettsial organism which was finally demonstrated to be the causal agent of the disease. The observations of Derrick and of Burnet were published in this journal on August 21, 1937; and subsequently, in the issue

of January 7, 1939, Derrick presented a formal description of the rickettsial agent and proposed that it be named *Rickettsia burneti*. Meantime a similar disease had been described in the United States in the State of Montana. On August 18, 1945, G. C. Morrissey and E. H. Derrick reported a case of "Q" fever occurring in northern Queensland. This was the first case recorded in Queensland occurring outside the southern part of the State; up till that time 217 cases had been diagnosed in southern Queensland. In reporting the case the authors remarked:

> One of the unsolved problems in the epidemiology of "Q" fever is the establishing of a link between the widely separated endemic centres of southern Queensland and Montana, U.S.A. The present case reduces the gap by a mere 500 miles. It is suggested that there may be a connecting chain of endemic centres along the eastern coast of Asia and adjacent islands.

It is of interest now to see reports of an outbreak in the United States of an apparently identical disease. Norman H. Topping, Charles C. Shepard and J. V. Irons[1] describe the epidemiological features. The outbreak, which was "explosive" in character, occurred in Amarillo, a city of 70,000 inhabitants situated near the centre of the "panhandle" in the State of Texas. Amarillo is an important centre for the livestock industry, and all the cases occurred during March, 1946, among people concerned with the handling or killing of livestock or the subsequent packing of meat. There were 55 cases and two deaths among 136 individuals obviously exposed, an attack rate of 40%. The inference is drawn that immunity was lacking in this group and that this was probably their first effective exposure to the disease, although they were mostly employed regularly in this type of work. The mode of infection is in doubt. No evidence was obtained implicating arthropods or indicating spread from person to person. A high infection rate occurred among those handling freshly killed meat in a packing plant, the onset of all their illnesses being concentrated into a short period of nine days; among those in contact with living stock the onset was spread over a much longer period which preceded and outlasted the outbreak in the packing plant. It is suggested that the infectious agent may have been in the dust of the stockyards, coming possibly from the excreta of the cattle. It was probable that cattle, in themselves apparently healthy, were the source of the human infections. Australian workers have, of course, suggested that the infectious agent in the dust is associated with the dried fæces of infected cattle ticks.

The clinical manifestations of the disease, described by J. V. Irons and John M. Hooper,[2] differed little from those first recorded by Derrick, notably fever, headache, and constitutional disturbances without the rash characteristic of typhus; the only distinctive feature was the frequent occurrence of pulmonary lesions, but most of these were of the broncho-pneumonic type and were detected by X-ray examination, not clinically. The severity varied greatly; some patients had very mild illnesses, two died. Sulphonamide and penicillin therapy was ineffective.

The diagnoses were confirmed serologically in the majority of cases, the antigen used being prepared from a strain isolated in 1935 from *Dermacentor andersoni* in Montana. This work was done by J. V. Irons, J. N. Murphy, junior, and Don M. Wolfe,[3] who comment that the results indicated that the complement-fixation test was both sensitive and specific. Its value was, however, more for retrospective diagnosis, as titres were at a low level during the first week of illness, but later generally reached high levels and maintained these for several weeks. The isolation of the organism is described by Herald R. Cox, Walter C. Tesar and J. V. Irons.[4] A rickettsial agent apparently identical in all criteria with *Rickettsia burneti* was recovered from the serum of each of the only two patients who were so investigated. It is emphasized that serological tests are preferable to attempts to isolate *Rickettsia burneti* because of the extreme infectiousness of this agent in the laboratory.

[1] *The Journal of the American Medical Association*, March 22, 1947.
[2] *Ibidem*, page 815.
[3] *Ibidem*, page 819.
[4] *Ibidem*, page 820.

The comment is made by the authors of the paper on the clinical data that the Amarillo epidemic of "Q" fever represented "the first sizable outbreak of this disease acquired naturally in the United States". In their opinion, it is becoming increasingly clear that "Q" fever must require consideration in the investigation of atypical and non-bacterial pneumonia and undiagnosed febrile illnesses. How far these remarks apply in Australia is, as yet, difficult to decide. As far as is known all reported cases occurring naturally, except one, have occurred in a circumscribed area. If they have occurred elsewhere they have presumably been unrecognized. In passing it is pleasing to see that Derrick's original suggestions for a name for the disease ("'Q' fever") and a designation for the causal agent (*"Rickettsia burneti"*) have apparently become accepted usage in the United States.

THE TREATMENT OF EPILEPSY.

IN the present state of our knowledge of the treatment of epilepsy and epileptiform conditions, the control of seizures has received more effective attention than the elucidation and treatment of essential causes. However, success even in the control of seizures has been far from complete, and many new drugs and methods aimed at this object have been introduced from time to time—mostly to be discarded after trial. One of the most promising of recent drugs is 3,5,5-trimethyloxazolidine-2,4-dione ("Tridione") to which reference was made by K. B. Noad in a paper published in this journal on July 5, 1947. Accumulated evidence from its use in the United States seems to have established its value so that more detailed description of its properties and use seems justified. This is available in a paper by William G. Lennox, of the Department of Neurology of Harvard Medical School,[1] in which he reports the results of the treatment with "Tridione" of 166 patients having a *petit mal* type of seizure, and also the results in the treatment of 93 patients having psychomotor or *grand mal* seizures. By the term *petit mal* Lennox does not refer to short-lived or mild seizures of any sort, but to three clinically distinct manifestations: *petit mal* (or pyknolepsy)—transient but frequent lapses of consciousness; myoclonic jerks; and akinetic (loss of posture) seizures. All three seizures, he states, are usually accompanied by the alternating spike and slow wave of the electroencephalogram. The results in the control of seizures in the *petit mal* triad were striking. Of the 166 patients, 31% became entirely free of seizures, 32% experienced a decrease in the number of seizures to less than one-fourth of the original number, and 20% were improved to a lesser extent; of the remainder, 13% were unchanged and 4% experienced an increase in the number of attacks. These patients had been previously treated with a variety of drugs, but in no case had complete relief been obtained, and only a limited number had been benefited by one or other of these drugs. The proportion of children who were freed of *petit mal*, but also (because of cerebral pathology) the proportion of those not helped at all, was greater for younger than for older children. Results were equally good for all three types of the *petit mal* triad. Great frequency of seizures was no bar to success of treatment with the drug.

The results in the treatment of *grand mal* seizures were quite discouraging; of 58 patients, 21% had less frequent and 50% had more frequent convulsions; in certain cases the drug appeared to produce a serious (even disastrous) aggravation of the condition. The second group of this type consisted of 35 patients suffering from psychomotor seizures, which are described as consisting of "a period of amnesia without convulsive movement other than possibly some tonic rigidity of muscles"; the impression gained from this small series was that "Tridione" alone was ineffective, but in a minority of cases it supplemented the therapeutic action of diphenylhydantoin sodium. In the case of patients suffering from both *petit mal* and *grand mal*, the results were more difficult to assess, but the conclusion seems to be that, in such cases, "Tridione"

[1] *The Journal of the American Medical Association*, May 10, 1947.

should be tried in combination with an appropriate anticonvulsant drug.

"Tridione" is dispensed in capsules, each of which contains 0·3 gramme. The beginning dose per day for infants is 0·3 gramme; in children, aged two to four years, 0·6 gramme; in those aged five years and above, 0·9 gramme. The usual dose for adults is 0·9 to 1·2 grammes daily. If after one month seizures are not controlled the daily dose is increased by 0·3 gramme at monthly intervals until therapeutic relief is secured, toxic symptoms appear or double the initial dose is being taken. Several of the patients treated by Lennox became free of seizures after the first dose, but maximum improvement usually occurred in from one to four weeks. In one case *petit mal* did not disappear until after six months' treatment with increasing doses of the drug. Of various side effects observed, rash and photophobia were most frequent. The most serious effect was the indication of toxic action on the bone marrow; the risk of this is possibly no greater than that associated with a number of other established drugs, but it must be borne in mind and monthly blood examinations made, the medication being discontinued if the number of neutrophile cells falls below 1,600 per cubic millimetre. The author also mentions reports of three cases of toxic amblyopia (which cleared when medication was stopped) and of four deaths from aplastic anæmia; two of Lennox's patients (neither of them suffering from *petit mal*) died during *status epilepticus* following administration of the drug.

It is presumed that "Tridione" will be available in this country before long. There seems little doubt from Lennox's report that it has a valuable place in the treatment of the *petit mal* triad, but it must be used with discretion. It is apparently contraindicated in the treatment of patients with convulsions (*grand mal* or psychomotor seizures) only. It must be used circumspectly or in combination with an anticonvulsant drug if the patient has both *petit mal* and convulsive seizures. Lennox thinks that it is the drug of choice in the treatment of the *petit mal* triad. This may be true, but the wise clinician will maintain a healthy scepticism and reserve his judgement; when he does use the drug he will see that its administration is carefully controlled and that adequate clinical and laboratory checks are maintained.

ULCERATIVE COLITIS.

ULCERATIVE COLITIS is one of the resistant chronic diseases about whose causes there has been much argument, and about whose prognosis there has been considerable though probably excessive pessimism. Three papers read before the Section of Gastroenterology and Proctology at the ninety-fifth session of the American Medical Association are of value as they present some of the more encouraging ideas.[1]

B. B. Crohn, J. H. Garlock and H. Yarnis describe regional colitis, a form stated to account for 8% of all cases. The important point is that the rectum is free of the disease, and therefore sigmoidoscopic examination, usually relied upon to give evidence of the condition, will reveal nothing abnormal. The regional process may involve any part of the colon from caecum to sigmoid, and indeed the terminal portion of the ileum may also be involved. Eventually the affection spreads to the remaining part of the large bowel, so that the early problem of dealing with a pathological process in the ascending or transverse colon becomes the more formidable one of treating a much larger area. Many cases have been reported, the right side of the colon being chiefly affected in the earlier stages, but recognition of regional colitis has been often delayed because of the much less pronounced local symptoms. Urgency, straining and blood-stained flux are less conspicuous, and accurate diagnosis is made only by radiological means. Obstruction, abscesses and fistulæ may occur, and also gross bleeding, as in the generalized form. More striking are the metastatic symptoms. Joint involvements are common, and uveitis and iritis also are seen as in bacillary dysentery. The results obtained by these authors have been encouraging. Medical measures included retention enemata of neutral acriflavine in isotonic solution, and the administration of succinylsulphathiazole, or the newer phthalyl combination. As these drugs have a low absorption rate they were continued more or less indefinitely unless any toxic symptoms appeared. Only 15% of the patients were cured by this treatment, and after a trial of medical methods most of them were treated surgically. Even with a total mortality of 20% among the patients submitted to operation, it is claimed by the authors that the good end results in most instances and the inevitability of subsequent spread of the disease, unless drastic measures are adopted, justify their procedures. Of the 46 patients who recovered only three have shown any evidence of recurrence or spread of the colitis. The operation of choice was a preliminary ileo-sigmoidostomy, followed at a later date by a subtotal excision of the colon. If the desired site of anastomosis was not healthy, ileostomy alone was performed for the time being. These authors lay stress on the favourable results which may be obtained if the disease is recognized in its purely regional form and courageous treatment is adopted. Attention to various technical points in operation is producing a definite drop in the mortality rate.

The next communication concerns the results of the oral administration of penicillin to patients with chronic ulcerative colitis, by M. H. Streicher. This writer comments on the greater success obtained in recent years by the use of the less freely absorbed sulphonamides. The specific properties of penicillin led him to give an extensive trial to penicillin given by mouth, in spite of the claims that inactivation takes place in the alimentary tract, and he reports encouraging results. Doses from 100,000 to 300,000 units per day were administered for periods of from one to four weeks. The effect on the coliform organisms was doubtful, but inhibition of the other Gram-positive organisms was observed. Estimation of the penicillin levels in the stools, blood and urine showed that the penicillin was not entirely inactivated in its passage through the digestive tract, some of the figures obtained being much higher than might have been expected. The clinical results were judged to be good. A series of 45 patients was observed over a period of one year; though it was found that the results were better when phthalylsulphathiazole was given simultaneously, it was believed that the penicillin was responsible for definite clinical improvement. As was pointed out in the discussion on these papers, judgement must be suspended as yet, for disappointments have followed initial apparent successes in this disease before now.

The last paper dealt with the causes and management of anæmia in ulcerative colitis. Anæmia has long been recognized as a very significant feature of the disease; it is usually of the microcytic type, and has been thought to be due to loss of blood and iron, and to nutritional deficiencies. H. M. Pollard, M. Block and W. H. Bachrach in a survey of 109 patients tried to estimate the importance of a number of causal factors, such as deficiencies in red cells, in iron and in general nutrition giving rise to weight loss and a lowered level of serum proteins, infection producing signs of toxæmia such as fever, and the duration and anatomical extent of the disease. No comprehensive or dogmatic statement can cover all these factors, but it is clear from their observations that all these must be considered. Treatment of the anæmia is to a great extent wrapped up in the treatment of the disease. More severe degrees of anæmia were found in women than in men. Occasional difficulty was found in the administration of iron, but an enteric-coated tablet of ferrous sulphate gave little trouble. Blood transfusions were given to some patients, who had suffered severe blood loss, but it has been found by a number of other observers that the value of transfusion in this condition does not seem to correspond quite to the restoration of the blood level alone. While no striking advances are described in these papers, there is evidence of greater activity in attack against a disease that is not only crippling, but also potentially fatal unless early and sustained efforts are made to defeat or limit its inroads not only on the colon alone, but on the whole bodily economy.

[1] *The Journal of the American Medical Association*, May 24, 1947.

Abstracts from Medical Literature.

MEDICINE.

Hypertension.

R. K. RATLIFF, R. M. NESBIT, R. T. PLUMB AND W. BOHNE (*The Journal of the American Medical Association*, February 1, 1947) discuss nephrectomy for hypertension. All hypertensive patients at the University of Michigan Hospital are fully investigated for renal function, and in all cases excretory pyelograms are prepared. If these are not satisfactory, cystoscopy and retrograde pyelography with split phenolsulphonephthalein are carried out. Congenital absence of a kidney, reduplication of a renal pelvis and bilateral renal lesions occurred in 70 out of 2,055 hypertensive patients. Unilateral lesions were reported in 113 patients. Interpretation is difficult. In the United States of America there was a great tendency to diagnose abnormal conditions in early years, which has now subsided to some extent; forty-nine patients were operated on in eleven years. Their systolic blood pressures were over 200 millimetres of mercury and diastolic pressures over 100. Chronic pyelonephritis, hydronephrosis and pyonephrosis comprised the findings in 43 of the 49 cases. Results were good in 17 cases. Adult patients did better than juvenile pyelonephritics.

Tongue Prints.

J. R. DI PALMA (*Archives of Internal Medicine*, October, 1946) describes a method of recording the state of the surface of the tongue. An inking solution is made by heating at boiling temperature for ten minutes in a water bath two grammes of Evan's blue and ten grammes of acacia in forty millilitres of distilled water. When the solution is cool a few drops of chlorbutol may be added to prevent the growth of moulds. The solution, which is odourless, tasteless and non-poisonous, is spread with a piece of gauze on the tongue, which is protruded in a relaxed state one inch from the teeth, the excess is blotted off with another piece of gauze, and prints are made by pressing pieces of thick glazed paper, four inches square, gently but firmly onto the tongue.

Arsenical Poisoning.

M. H. SULZBERGER AND R. L. BAER (*The Journal of the American Medical Association*, February 1, 1947) discuss the treatment of arsenical poisoning and especially dermatitis with BAL (dimercaprol). This preparation was discovered and tested in England. It was found that both animals and men could be protected against arsenical vesicants by application of BAL to the skin before and even up to two hours after the vesicant was applied. In arsenical dermatitis due to antisyphilitic drugs, inunction with BAL ointment or intramuscular injection of BAL (5%) in peanut oil with benzyl benzoate (10%) produced complete recovery of 80% of patients in thirteen days. The longer the duration of the dermatitis before treatment with BAL, the longer the time for improvement. Of other toxic effects of arsenical treatment, toxic encephalitis, agranulocytosis, aplastic anæmia, jaundice and arsenical fever were all found to respond to the use of BAL. The doses recommended in severe cases are three milligrammes per kilogram every four hours on the first two days, four times on the third day, and twice a day for the next ten days, or until complete recovery occurs. In mild cases a dose of 2·5 milligrammes per kilogram is given four times a day for two days, twice on the third day, and once or twice a day thereafter till recovery is complete. Toxic effects of the treatment may be nausea, vomiting, burning in lips and mouth or extremities, constriction of throat and chest, and rise of blood pressure about fifteen minutes after the injection of BAL. Barbiturates are used for these symptoms. Local abscesses occurred at the site of injection of BAL in some cases, and in a series of 131 cases of serious complications of arsenical treatment, 5% of patients died. These are considered good figures in view of the severity of the lesions.

Nephritic Œdema and the Retention of Salt.

H. GRANT AND F. REICHSMANN (*American Heart Journal*, December, 1946) have shown that normal adults exhibit abnormal hydration when large quantities of sodium chloride (of the order of 20 to 30 grammes daily) are fed to them. The blood volume, venous pressure and extracellular fluid volume are increased, much as in congestive heart failure. The authors suggest that the œdema in those patients with acute glomerulonephritis who do not exhibit pulmonary congestion, gallop rhythm or prolonged circulation time is due to the retention of salt and water by the diseased kidneys.

Epidemic Encephalitis.

A. B. SABIN (*The Journal of the American Medical Association*, February 1, 1947) describes a number of cases of epidemic encephalitis due to the Japanese B virus on Okinawa in 1945. In the first place a number of natives and later twelve members of the military forces developed the disease. Drowsiness, lethargy, mental confusion and semi or complete coma, with high fever, nuchal and spinal rigidity, leucocytosis and pleocytosis, were observed. Neutralizing antibodies were found in the patients' serum within three days of the onset of symptoms. Neutralization and complement fixation tests established a specific serological diagnosis in nine cases among Americans. Japanese B encephalitis mouse brain vaccine was administered to 250,000 persons (two or three doses). No case of demyelinating encephalopathy occurred.

Use of Sulphadiazine in the Presence of Hæmaturia.

JOSEPH N. NICHOLSON (*The New England Journal of Medicine*, September 12, 1946) has observed a series of 66 cases of meningococcal meningitis treated with sulphadiazine to determine the indications for cessation of the treatment as far as renal lesions are concerned. An initial dose of four grammes followed by two grammes every four hours was given orally when possible; alternately an initial intravenous dose of five grammes of sodium sulphadiazine was given, followed by further doses of 2·5 or 5·0 grammes, depending on the blood level, as much as 20 grammes being given in the first twenty-four hours in some cases. The urine was made and kept alkaline either by oral administration of sodium bicarbonate in 2·5 gramme doses in the first twenty-four hours, or by the intravenous administration of 1,100 millilitres of one-sixth molar sodium lactate solution. Some variation in these doses was determined by the pH of the urine. Adequate hydration was maintained by the administration of at least 3,000 millilitres of fluid and a urinary output equal to at least 50% of the intake of fluid. Of fifty patients in the series in which sodium bicarbonate was used, four showed microscopic and eight gross hæmaturia. In the remaining sixteen cases sodium lactate solution was used, and two instances of gross hæmaturia occurred. In the author's opinion this did not indicate a need for cessation of treatment, which was continued, but only in the presence of alkaline urine and adequate output. Under these conditions the hæmaturia actually disappeared during treatment, so it is concluded that hæmaturia is not a contraindication to the continued use of the drug provided that the urine is kept alkaline and the fluid balance maintained.

Gall-Bladder Disease.

M. FELDINAN (*American Journal of Digestive Diseases*, February, 1947) discusses the clinical significance of the sluggishly emptying gall-bladder as disclosed by X-ray examination. In 396 consecutive cholecystographs there were 75 in which sluggish emptying of the gall-bladder was reported, without the presence of calculi. The significance of this condition is not well understood. A variety of causes have been described by different authors. Operation in these cases often does not relieve the patient's symptoms, because it is not certain to what extent the condition is pathological. Eighteen separate causes of sluggish emptying are described by the author. These include adhesions, pylorospasm, spasm of the cystic duct, allergy, pregnancy, drugs, thick bile, thick mucus, duodenal ileus, pyloric obstruction, reflex, digestive disturbances, nervous dysfunction, kink of the neck of the gall-bladder, and changes in the wall of the gall-bladder. A fat stimulus empties the gall-bladder in three to five minutes. Nitroglycerin, amyl nitrite, atropine and "Syntropan" (25 milligrammes orally) did not accelerate emptying in the author's experience. Women were more often affected than men. Symptoms included acute attacks, abdominal and scapular pain, abdominal distension, nausea, vomiting. The appetite was good in the majority. Obesity and hypothyreoidism were often noted. The author lays stress on the necessity of a wide view in diagnosis. The individual habits and diathesis must be carefully considered and evaluated, and it must be borne in mind that the patient's symptoms may not be due to or associated with the sluggish gall-bladder.

Salmonella.

O. TELSENFELD AND V. M. YOUNG (*The American Journal of Digestive Diseases*, February, 1947) discuss geography of salmonella. There are about 150 types of salmonella, most of which cause primary infestation in animals and birds. These types can, however, be transferred to man by meat, eggs and other foods. There are five clinical salmonella syndromes: paratyphoid

disease, septicæmia, enteritis, localized inflammation and a symptomless carrier state. The organism is widely spread throughout the world and causes one or other of the salmonella syndromes in different localities. *Salmonellæ paratyphi* A and B are world wide and give rise mainly to salmonella fever. *Salmonella typhi murium* has been found in many different animals, including camels and foxes; it is the predominating salmonella in most parts of the world, including Australia and New Guinea. Often conveyed through fowls, eggs and custards, it usually causes only transient gastro-enteritis. *Salmonellæ Derby* and paratyphoid C are rare. *Salmonella cholera suis* (*Salmonella suipestifer*) is most dangerous, causes septicæmia mainly, and occurs all over the world, but more frequently in America and the Netherlands Indies. *Salmonella Thompson enteritidis* occurs in poultry and in duck eggs, mainly in Europe. *Salmonella Montevideo* occurs in healthy hogs and chickens and in sick fowls. *Salmonella Newport* and *Dublin* are prevalent in Denmark where ducks are infected. Rats, snakes, calves, animals for market meat, dogs, cows and humans can harbour and convey the organism. Diagnostic methods for detecting salmonella have to be modified according to the local strains. Most laboratories forward their salmonella strains to a salmonella centre for typing. The control of the disease is difficult and requires all the vigilance of the physician, the bacteriologist and the public health authorities.

Epidemic Neonatal Diarrhœa.

D. M. STERN (*The Lancet*, January 11, 1947) found from the study of an epidemic of neonatal diarrhœa in hospital that the only common factor of all the cases was the use of pooled feeding bottles and teats, and two further epidemics were checked by the substitution of spoon feeding for bottles. He suggests that infection may be spread by contamination of the film which forms inside feeding bottles which are in constant use, and that the risks of bottle feeding may be lessened by the keeping of a separate bottle and teats for each baby, or by sterilization of the bottles after they have been thoroughly cleansed of film. The teats, it is stated, cannot be sterilized without destruction.

Segmental Bronchitis.

E. RIST *et alii* (*La presse médicale*, March 15, 1947) have found by making bronchoscopic examinations that simple bronchitis is not always a diffuse and generalized affection of the bronchial tree, but that it often affects a relatively short segment of a large bronchus.

Thromboangiitis Obliterans.

N. S. FREEMAN (*American Heart Journal*, March, 1947) has assembled from three "vascular centres" attached to United States Army hospitals material relating to 274 patients suffering from *thromboangiitis obliterans*. The disease was usually seen in its earlier stages and intermittent claudication was the commonest leading symptom. In treatment excellent results were obtained from intravenous injections of typhoid vaccine, in amounts just sufficient to produce moderate fever, and ability to walk was improved by intramuscular injections of tissue extracts. Buerger's exercises and physiotherapy were not found to be very successful. Sympathectomy was the treatment of choice where there was evidence of increased vasomotor tone as determined by oscillometry and the measurement of skin temperatures after blocking the sympathetic vasoconstrictor pathways. A major amputation was necessary for only two patients during the observation period. The author places very great emphasis on the therapeutic value of abstinence from smoking by those patients who have been smokers of tobacco. Abstinence from smoking alone often results in a great alleviation of the disease and of such of its effects as pain and gangrene; but the abstinence must be total and permanent. Many patients are doomed because they are unable to give up tobacco or unable to persist in their resolutions to abstain from it.

Heart Block Diagnosed in a Fœtus before Birth.

F. C. JORDAN AND H. RANDOLPH (*American Heart Journal*, January, 1947) report the diagnosis of complete heart block in a fœtus five weeks before term by means of phonocardiograms. The diagnosis was confirmed after the birth of the child.

Rheumatic Mitral Valve Disease without Cardiac Enlargement.

BERNARD S. EPSTEIN (*Radiology*, March, 1947) states that loud and classical apical murmurs diagnostic of mitral valve disease may exist in the absence of cardiac enlargement or changes in the silhouette of the heart, just as it is possible for pronounced cardiac enlargement to be present with minimal and often misinterpreted murmurs. If the murmurs are characteristic, the diagnosis of mitral valve disease must be made even in the absence of any radiological criteria. Conversely, if there is any enlargement of the heart, the conclusion that organic heart disease is present must be reached. In the diagnosis of mitral valve disease the demonstration of left atrial dilatation is the earliest radiological sign. This may be obtained in patients with murmurs which by all description should be considered functional. On the other hand, there are many patients with classical mitral disease as indicated by pathognomonic murmurs who have no visible cardiac enlargement. There is also a small group of patients with mitral stenosis who have cardiac enlargement without left atrial dilatation. It should be recognized by both the radiologist and the clinician that in mitral valve disease there may be no visible alteration in the radiographic appearance of the heart, just as murmurs may be absent or atypical.

Hypertrophic Cirrhosis of Hanot.

A. O. WILENSKY (*The American Journal of Digestive Diseases*, February, 1947) discusses the cause and pathology of Hanot's hypertrophic cirrhosis of the liver. The author states that in this condition there are early and continuous jaundice, attacks of fever and leucocytosis, enlargement of the spleen and lymph nodes, and sometimes peritonitis. The jaundice is due to hæmolysis, especially in the spleen. The pancreas is affected by fibrosis and fatty changes and the lymph nodes show fibrosis, pigmentation and cellular invasion. The fact that the liver, spleen, pancreas and associated lymph nodes are affected suggests some common factor which may be found in the fact that all these organs are supplied with blood from the mesenteric axis. It is suggested that the disease is blood-borne, through the mesenteric axis; and the fever, leucocytosis and other evidence of inflammatory change suggest a blood-borne infection. The main changes are in the reticulo-endothelial structures and the condition should be regarded as a reticulo-endotheliosis.

Marble Bone Disease.

ACCORDING to Carla Zawisch (*Archives of Pathology*, January, 1947), marble bone disease is due to the influence of an unknown agent which damages the bone-forming blastema at the beginning of the second period of the development of each individual bone. From this time on, the differentiation of bone tissue is retarded and the less differentiated types become hyperplastic. The malformation is responsible for the general retardation of resorption, because the two phases of the bone-forming process—deposition and resorption—condition and stimulate each other. In marble bone disease the threshold of response to stimuli which bring about resorption is raised. Resorption is arrested at the beginning of the second period for a long time. The results are: fœtal size and shape of the marrow cavity, a thick cortex composed of all the embryonic strata which normally are removed, and an unusual amount of medullary bone. The clubbing of the ends of long bones is the result of the hyperplasia and persistence of less differentiated types of bone tissue in the metaphyses. The greater density of marble bones in the X-ray picture is due partly to a greater density of structure when the bones are in a state of repair (eburnation) and partly to a higher calcium content, revealed indirectly by the scarcity of fibrils in all the types of bone tissue involved. The anæmia in marble bone disease may be due to the agent which impairs the differentiation of bone tissue. It is more likely that it is due to the relative lack of a substance which normally is released by the resorption of bone and stimulates the hæmatopoiesis.

The Treatment of Perennial Allergic Rhinitis.

P. H. SPRAGUE AND T. H. AARON (*The Canadian Medical Association Journal*, December, 1946) report some experiences in the treatment of perennial allergic rhinitis. The report is based upon a study of 48 cases over a period of five years, in most instances. They emphasize the significant part in this disease played by contact with house dust and feathers as compared to other allergic substances. The serious complications of perennial allergic rhinitis, such as asthma, persistent cough, sinus complications *et cetera*, are referred to and tabulated. Permanent benefit from treatment is recorded in 43% of all cases, and it is considered that much of the permanency of the results obtained is due to the education of the patient in the significance of allergic contacts. A series of skin tests was carried out in all cases, and it was found impossible to implicate food as a certain causative factor. In the case of animal danders and feathers, the patient was advised to avoid contact, but in the case of house dust, a programme of desensitizing injections was prescribed.

Bibliography of Scientific and Industrial Reports.[1]

THE RESULTS OF WAR-TIME RESEARCH.

During the war a great deal of research was carried out under the auspices of the Allied Governments. It has been decided to release for general use a large proportion of the results of this research, together with information taken from former enemy countries as a form of reparations. With this end in view, the United States Department of Commerce, through its Publication Board, is making a weekly issue of abstracts of reports in the form of a "Bibliography of Scientific and Industrial Reports". This bibliography is now being received in Australia, and relevant extracts are reproduced hereunder.

Copies of the original reports may be obtained in two ways: (a) Microfilm or photostat copies may be purchased from the United States through the Council for Scientific and Industrial Research Information Service. Those desiring to avail themselves of this service should send the Australian equivalent of the net quoted United States price to the Council for Scientific and Industrial Research Information Service, 425, St. Kilda Road, Melbourne, S.C.2, and quote the PB number, author's name, and the subject of the abstract. All other charges will be borne by the Council for Scientific and Industrial Research. (b) The reports referenced with an E number may be obtained in approved cases without cost on application to the Secondary Industries Division of the Ministry of Post-War Reconstruction, Wentworth House, 203, Collins Street, Melbourne, C.1. Copies of these are available for reference in public libraries.

Further information on subjects covered in the reports and kindred subjects may be obtained by approaching the Council for Scientific and Industrial Research Information Service, the Secondary Industries Division of the Ministry of Post-War Reconstruction, or the Munitions Supply Laboratories (Technical Information Section), Maribyrnong, Victoria.

PB 40483. GIBSON, JOHN G., II, *et alii*. Resuspension of red cells in a modified acid citrate-dextrose solution with and without fraction IV, 3, 4, lot 301. (α and β globulin.) Bimonthly progress report, No. 25. June, 1945. 6 pp. Price: Microfilm, $1.00; Photostat, $1.00.

All donors were all Group O, Rh-positive. The cells were resuspended in the modified acid citrate-dextrose solution. These cell suspensions were transfused into individual recipients, nine of whom were Group O, four were Group A, and two were Group B, all Rh-positive. Transfusions were given up to as long as 38 days of storage. The number of days stored, the condition of the cell resuspensions at the time of transfusion as determined by in-vitro studies, and the percentage of survival as determined by the radioactive iron technique are shown in Table 1. The survival rate was shown to be better with the globulin-fortified solution. The report also describes the results obtained with the clinical use of cells resuspended in acid citrate-dextrose at the Peter Bent Brigham Hospital. The cells were all of Group O, Rh-positive donors. The number of days these cell suspensions were stored prior to transfusion, together with the data obtained from in-vitro studies done on samples of the blood on the day they were transfused, are shown in Table 2. Also shown are the results of determinations of the rise in total serum bilirubin four hours after receiving the transfusion. This report covers work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract OEMcmr-131).

PB 40484. GIBSON, JOHN G., II, *et alii*. Resuspended packed red cells. Bimonthly progress report, No. 26. August, 1945. 5 pp. Price: Microfilm, $1.00; Photostat, $1.00.

A study was made of the post-transfusion survival of cells taken as whole blood in ACD and stored at 4° C. after removal of plasma. All donors were Group O, Rh-positive. Each lot of packed cells was transfused into individual recipients after storage ranging from 9 to 21 days after collecting. In Experiment 115 the cells were transfused as packed cells; in the other four experiments normal saline solution was added. The results are given in Table I. It was concluded that the preservation of cells drawn as whole blood in ACD-1 is not as good after the removal of plasma as when the cells are stored as whole blood. Other experiments investigated the preservation of cells taken in 4% sodium citrate and resuspended in an acidified citrate-dextrose solution. The donors were Group O, Rh-positive, Wassermann negative. The cell resuspensions were transfused into individuals at 6, 10, 16 and 21 days after collecting. The data obtained are shown in Table 2. It was concluded that the solution was of little or no value as a preservative for cells drawn into 4% sodium citrate. This progress report covers work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract OEMcmr-131).

PB 40485. GIBSON, JOHN G., II, *et alii*. Transfusion of high anti-A titre Group O blood into Group A recipients. Effect of Vitebsky substance on preservation of blood in ACD-1. Bimonthly progress report, No. 27. October, 1945. 2 pp. Price: Microfilm, $1.00; Photostat, $1.00.

This report summarizes the results of two experiments in which high titre anti-A plasma only from Group O blood was given to Group A recipients. Donors and recipients were Rh-positive. The recipients were blood Group A subjects who had previously been built up with radioactive iron, Fe^{55}. Freshly drawn cells from another Group O donor who had been prepared with Fe^{59} were also given to the recipients. Both of the recipients were secreters of "A" substance. The plasma of the recipient without reaction contained agglutinins but no hæmolysins. It was concluded that significant destruction of recipient's A cells was not produced by administration of high anti-A Group O plasma in these subjects. Under the conditions of the other experiment, the addition of Vitebsky A-B soluble group-specific substance did not decrease the survival of cells taken as whole blood in acid tartrate. This report covers work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract OEMcmr-131).

PB 40463. GIESE, ARTHUR C., AND WELLS, JULIAN N. Sunburn protection. Bimonthly progress reports, Nos. 1-3. August-December, 1943. 7 pp. Price: Microfilm, $1.00; Photostat, $1.00.

Results of attempts to increase the resistance of human skin to ultra-violet light are summarized in these reports. Thickening of the corneum or horny layer of the skin by chemical means did not prove feasible. The chemicals tried were mainly protein precipitants (acetone, 5% and 20% formalin, 20% chromic acid, picric acid, tannic acid, 5% mercuric chloride *et cetera*). In addition, hardening agents (tincture of benzoin, saturated aqueous alum, saturated ether solution of rosin) were tried. A saturated aqueous solution of calcium chloride was also tried. Tables show the effects of chemicals on mouse skin, frog skin and chick skin. The reports also give the results of attempts to develop a satisfactory sweat-resistant ointment for sunburn protection. After trying many combinations, magnesium stearate was selected to improve adhesiveness and water repellent properties, diethylphthalate for uniform spreading and some surface tension lowering, and mineral oil to give a smoother texture. Sodium lauryl sulphate was found to assist in removing the ointment from the skin on washing. These progress reports cover work performed under the auspices of the Committee on Medical Research, Office of Scientific Research and Development.

PB 40466. GIESE, ARTHUR C., AND WELLS, JULIAN M. Sunburn protection: Efficiency of sunburn preventive ointments. Bimonthly progress report, No. 3 (final report). (OSRD CMR Clinical Investigation Report 43.) February, 1944. 8 pp. Price: Microfilm, $1.00; Photostat, $1.00.

In this report the tests for sweat resistance and other properties of the various sunburn preventive ointments developed by these investigators are summarized and compared to two representative commercial ointments. After some preliminary trials only two sunscreens were chosen for further study: "HMS" (homomenthyl salicylate) and "PAB" (ethyl *p*-aminobenzoate (benzocaine)); as scattering agent TiO_2 was chosen, since it is non-toxic, effective and does not have undesirable properties. A table lists the various ointment bases that were considered. The sweat resistance, water resistance and abrasion resistance of various ointments are also tabulated. This final report covers work performed under the auspices of the Committee on Medical Research, Office of Scientific Research and Development.

PB 40465. GIESE, ARTHUR C., AND WELLS, JULIAN M. Sunburn protection: Ointment bases for sunscreens. Interim report, No. 2. (OSRD CMR Clinical Investigation Report 35.) February, 1944. 6 pp. Price: Microfilm, $1.00; Photostat, $1.00.

This report summarizes the results of efforts to obtain a satisfactory ointment to act as a sunscreen for sunburn protection. The ointments tested were mainly of the vanishing cream and fatty or greasy base types. Several formulæ are given which have almost all of the desired properties. Among the ingredients listed are the following:

[1] Supplied by the Information Service of the Council for Scientific and Industrial Research.

titanium dioxide, magnesium oxide, magnesium stearate, butyl stearate and ethyl *p*-aminobenzoate (benzocaine). Work is still in progress on ointments which formed good films and had good water resistance. This report covers work performed under the auspices of the Committee on Medical Research, Office of Scientific Research and Development.

PB 40492. GREELEY, PAUL O. Explosive decompression. Progress reports, Nos. 1-6. December, 1942, to October, 1943. 8 pp. Price: Microfilm, $1.00; Photostat, $1.00.

These progress reports summarize the findings of various experiments on animals to determine the effects of explosive decompression. Experiments on rats and rabbits were made in order to determine outward appearances and changes in lung volume. Other experiments were set up to determine whether the variation in results had any relationship to the phase of respiration. Fifteen decompressions were carried out on one dog using various pressure differentials and various decompression rates. Over three hundred rats were explosively decompressed and autopsied in order to determine the factors responsible for pathological changes. Explosive decompressions were also carried out on rats which were protected from freezing by jackets. One of these tests is described more fully in PB 40493 under W. E. Berg. The progress made in the construction of a large decompression and cold chamber is also noted. A few tables are included; however, the tables to report 2 are lacking as is a diagram to report 1 of a gate valve. These progress reports cover work performed under the auspices of the Committee of Medical Research of the Office of Scientific Research and Development (Contract Nos. M-1910 and OEMcmr-258).

PB 40495. GROLLMAN, ARTHUR. Adrenal cortical substitutes. Monthly progress reports, Nos. 1-4. February-May, 1942. 4 pp. Price: Microfilm, $1.00; Photostat, $1.00.

These very brief progress reports merely mention the use of natural products (*Digitalis purpurea, Digitalis lanta,* squill, strophanthus) which have been hydrolyzed and tested on adrenalectomized rats. Very few findings are given. The titles for reports 3 and 4 are "Preparation of Synthetic Compounds of Adrenal Cortical Hormone". These progress reports cover work under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract Nos. M-709 and OEMcmr-95).

PB 40496. GROLLMAN, ARTHUR. Preparation of synthetic compounds of adrenal cortical hormone. Monthly progress report, No. 3 (final report). June, 1942. 1 p. Price: Microfilm, $1.00; Photostat, $1.00.

This final report very briefly summarizes the investigation of steroids derived from various naturally occurring glucosides which were studied for their adrenocortical-like and salt-retaining capacity. None of these proved to be of any material effectiveness for this purpose. No details are included in this study. This report covers work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract No. OEMcmr-95).

PB 40554. HUTCHENS, JOHN O., *et alii.* Improved microapparatus for controlled toxicity determinations. Progress report, October 4, 1943. (OSRD Report 2047; Chicago University Toxicity Laboratory Report 37.) November, 1943. 20 pp. Price: Microfilm, $1.00; Photostat, $2.00.

This report contains a description of an all-glass system, made up of a chamber and accompanying air and vapour supply apparatus, suitable for the exposure of small animals to toxic vapours. It has a number of advantages over a small-scale apparatus previously described (Toxicity Lab. Rept. 6, OSRD Rept. 580, PB 5569, see Vol. 1, p. 454, this bibliography) with respect to ease of manipulation, number of animals exposed, insurance of even exposure of all animals, and the control of humidity and rate of air flow. Apparatus accessory to the chamber provides for the exposure of bodies only; and a special manifold for exposure by respiration only is described. Photographs and diagrams of the apparatus are included.

PB 40357. GUSTAVSON, REUBEN G. Effect of sterols and anoxia. Monthly progress reports, Nos. 1-8. March-December, 1942. 11 pp. Price: Microfilm, $1.00; Photostat, $1.00.

Several of these progress reports compare the effects of œstrone, testosterone propionate, pregnanediol and vitamin *D* to anoxia, the pregnanediol being the only one not increasing the resistance to anoxia. The animals submitted to anoxia in general seemed to show a decrease in the amount of colloid present and a definitely higher follicular epithelium. Other experiments studied the resistance to anoxia by a different method. Testosterone, œstrone and diethyl stilbœstrol were injected into animals which were then placed in a chamber with reduced pressure instead of a nitrogen dilution chamber as in the other experiments. Diethyl stilbœstrol decreased the resistance of the animals to hypoxia. In all cases, the injected animals showed some degree of cortical degeneration. Damage was most consistently found in the *zona fasciculata.* Œdema, hæmorrhage, hyperæmia, all stages of nuclear degeneration, and fatty degeneration were consistent findings in this group. A table shows the findings of the study of the basal metabolic rates of œstrone-treated animals. A statistical analysis was also made of the tests using diethyl stilbœstrol. Other tables are included. These progress reports cover work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (Contract OEMcmr-64). Report No. 1 is poorly reproduced.

PB 40371. LINCOLN, RALPH E., *et alii.* Respiratory pathogenicity of *Bacillus anthracis* spores: III. Changes in pathogenicity due to nutritional modifications. 1946. 31 pp. Price: Microfilm, $1.00; Photostat, $3.00.

Repeated experiments have shown that the respiratory pathogenicity of *Bacillus anthracis* spores produced in media containing corn steep liquor (CSL) is decreased to about one-third that of spores produced in media not containing CSL. The loss in pathogenicity is regained when spores of lowered pathogenicity are again grown in CSL-free media. These changes in pathogenicity are due to temporary alterations in the expression of the genetic constitution of the culture rather than to changes in genetic constitution. From tests in which mineral and carbohydrate constituents of the media were varied, it appears that an interaction of carbohydrate and mineral metabolism may be at least partly responsible. From the results of subcutaneous tests upon rats, it is certain that no diminution in subcutaneous pathogenicity occurs. This would indicate that whatever the nature of the change may be, it alters the respiratory pathogenicity by affecting the invasiveness of the spores. Tables and bibliography are included. This work was carried out at Camp Detrick, Frederick, Maryland.

PB 40965. MILLER, ROGER G. Study of materials and processes for artificial replacement of mutilated parts of the body. Monthly progress reports, Nos. 1-5, 7-10. March, 1942, to January, 1943. 9 pp. Price: Microfilm, $1.00; Photostat, $1.00.

These progress reports record the progress made under this project for artificial replacement of mutilated parts. Several materials, including vinylite resins, latex and sponge rubber, were under consideration. Most promising of these materials at this stage was a sponge rubber which was strong, tough and resistant to deterioration. For additional progress reports and final report see PB 40967-PB 40969. These progress reports cover work performed under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development (M-624). Roger G. Miller was with the Dental Corps, United States Army.

PB 40368. NEWBURGH, L. H., AND SPEALMAN, C. R. Acclimatization to cold. (National Research Council. Committee on Aviation Medicine Report 241.) December, 1943. 11 pp. Price: Microfilm, $1.00; Photostat, $1.00.

Three young men lived for two weeks and four other young men lived for four weeks in a room whose air temperature was 15° C. (59° F.). Under the conditions of the experiment this temperature was low enough to cause distinct and continued discomfort, but not cold enough to cause shivering. A slight increase (about 7%) in both basal and total heat production occurred after ten or more days. In some instances there was a little further increase with time; in others the augmented heat production lasted for a number of days after the subjects were released from the cold. This delayed onset of increase in heat production suggests that it is the result of augmented thyreoid activity. Slight lowering of blood cholesterols tends to support this explanation. The discomfort due to cold gradually lessened or disappeared. This was not due to change in skin temperature or to increased heat production. Tabulated data and a graph showing the basal metabolic rate are included, together with a bibliography. This report covers work performed at the Naval Medical Research Institute, Bethesda, Maryland, under contract with the University of Michigan Medical School (OEMcmr-269).

PB 40372. YOUNG, GEORGE A., JUNIOR, AND ZELLE, M. R. Respiratory pathogenicity of *Bacillus anthracis* spores: IV. Chemical-biological synergisms. 1946. 16 pp. Price: Microfilm, $1.00; Photostat, $2.00.

Respiratory exposure to mixed "Aerosols" of heavy metals and *Bacillus anthracis* spores in concentrations which would have had no lethal effect if used separately causes fatal anthrax infections in mice, guinea-pigs and rats. This relationship between the chemicals and anthrax spores is truly synergistic. An hypothesis is presented attributing the synergism to chemical inactivation of the enzyme systems which are dependent upon the presence of free sulphhydryl groups for their activity. Tables and bibliography are included. This work was carried out at Camp Detrick, Frederick, Maryland.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on April 17, 1947, at the Royal Alexandra Hospital for Children. The meeting took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital. Part of this report appeared in the issue of July 12, 1947.

Diaphragmatic Hernia.

DR. LAWRENCE HUGHES presented a male patient, aged seventeen months, who had been admitted to hospital on March 13, 1947, with the history that for six months he had been very difficult to feed. He had taken fluids, but could take only small quantities of solid foods, and these he held in his mouth for long periods. He vomited when any attempt was made to force food. He had made very little gain in weight, gaining only eight to ten ounces in the previous six months. He was becoming increasingly pale. Examination of the chest revealed that his heart and mediastinum were displaced to the right; there was dulness in the lower part of the left side of the chest with audible peristaltic sounds. X-ray examination following a barium meal showed a left diaphragmatic hernia. The lower part of the left side of the thorax was occupied by intestines, mainly small bowel, but colon was also present.

Rheumatic Carditis.

Dr. Hughes's second patient was a Chinese girl, aged seven years. She had been admitted to hospital at Vila in the New Hebrides in November, 1946, with a history of pain in the abdomen and joints for three weeks. On examination she was found to have an enlarged heart with the apex beat in the nipple line in the sixth left intercostal space. A loud systolic murmur was audible at all areas with its maximum intensity at the apex. Her temperature was 99·6° F. and her pulse rate 140 per minute. Her throat was injected, one knee was swollen and there was slight œdema of both ankles. Physical examination otherwise revealed no abnormality. She was given salicylates, and mild pyrexia continued for four weeks. The tip of her spleen became palpable during this period.

The child had been admitted to the Royal Alexandra Hospital for Children on March 21, 1947. At that time her temperature was normal and it had remained so ever since. She was orthopnœic. Her ankles were swollen and the veins of her neck were distended. Her general nutrition was good. The systolic blood pressure was 100 millimetres of mercury and the diastolic pressure 65 millimetres. The pulse rate varied between 120 and 140 per minute. Her heart was greatly enlarged; the apex beat was diffuse and was in the seventh left intercostal space just beyond the anterior axillary line. A loud systolic murmur was audible over most of the thorax and loudest at the apex. The liver was enlarged, being palpable three fingers' breadth below the costal margin, and had increased in size since her admission to hospital. The spleen was not palpable. During the few days preceding the clinical meeting she had developed ascites. The urine contained a trace of albumin. Examination of the blood revealed a total red blood cell count of 4,350,000 per cubic millimetre and hæmoglobin value of 12·5 grammes *per centum*. X-ray examination revealed enormous enlargement of the heart, particularly of the left auricle and ventricle. An electrocardiographic examination showed bifid *P* waves and marked right-sided preponderance.

Burns with Cerebral Complications.

The third patient presented by Dr. Hughes was a male child, aged twenty-one months. Birth had been normal. He had suffered from measles six months previously, but without complications, and had completely recovered. There was nothing significant in the family history. The child had been admitted to Goulburn Hospital on January 29, 1947, with severe first and second degree burns involving about 50% of the body surface. The injury had been sustained by his being pushed into a bucket of boiling water. He had been treated with fluids administrated intravenously, with penicillin and with sulphadiazine. The temperature, which had been raised, returned to normal in the second week and he had begun to improve. This improvement had been maintained, drugs had been discontinued, and during the fifth week the child was bright, eating well and playing in his bed. During the sixth week there had been slight diurnal rises of temperature, and one morning the child was found lying still in his bed with forcibly flexed arms and extended legs, not recognizing his parents, but periodically grimacing and uttering a high-pitched shriek. His urine at this time had contained a little sugar and up to one-quarter albumin. No jaundice had been noticed. The child had been admitted to the Royal Alexandra Hospital for Children on March 15, 1947, when the burns were found to be well healed with scarring, but his general condition was one of emaciation. He was lying flat on his back making involuntary movements; occasional slight twitching of the limbs and facial grimaces occurred. He appeared to be unconscious of his environment. Swallowing, yawning and champing movements of the jaws were observed periodically. He appeared to have very little, if any, vision; the pupils were moderately dilated and reacted sluggishly to light. His arms were held in abduction with the forearms strongly flexed; the spasticity could be overcome with prolonged pressure, the tone in the right arm appearing greater than that in the left. The legs were extended and spastic, but the tone varied from time to time. The tendon reflexes were exaggerated, the abdominal reflexes were absent, and the plantar reflexes varied, being sometimes flexor and sometimes extensor on either or both sides. The trunk was extended and the neck was held usually to one side. The tone of the limb muscles was not affected by posture or neck movements. Examination of the *fundi oculorum* revealed no abnormality. The condition of the skin sensation was difficult to assess, but there appeared to be anæsthesia to pin prick up to the level of the upper part of the thorax. The child's posture suggested a transverse spinal lesion at the level of the seventh cervical vertebra. Examination of the other systems revealed no abnormalities apart from a possible diminution in the extent of liver dulness. The child did not take fluids or solids well for the first few days after admission and required the intravenous administration of fluids including four ounces of blood. Since then he had taken food well. The general state of his nutrition had improved, but there did not appear to have been any marked change in the neurological state apart from transient variations in the muscle tone and in the state of the plantar reflexes. Examination of cerebro-spinal fluid on March 16, 1947, revealed that it was under a pressure of 110 millimetres of fluid. It contained one mononuclear cell per cubic millimetre, 720 milligrammes of chloride and less than 15 milligrammes of protein per 100 millilitres. Sugar was present. Further examination of the cerebro-spinal fluid on March 21, 1947, showed no change. A blood count on March 18, 1947, revealed 3,400,000 red blood cells per cubic millimetre and hæmoglobin value of 10·3 grammes *per centum*; 18,300 white blood cells per cubic millimetre were present, of which 84% were neutrophile cells, 13% lymphocytes and 2% eosinophile cells. Examination of the blood on the child's admission to hospital had showed the following additional values in each 100 millilitres: urea content 26 milligrammes, sugar content 80 milligrammes and serum protein content 6·5 grammes. X-ray examination of the cervical and thoracic vertebræ revealed no abnormality. The provisional diagnosis was demyelination following burns.

Acholuric Jaundice.

Dr. Hughes then presented a female child, aged five years, who had been admitted to hospital on October 31, 1946, with a provisional diagnosis of meningitis following a history for the previous twenty-four hours of fever, increasing headache, vomiting and finally convulsions. On examination, however, signs of pneumonia were found at the apex of the right lung, and it was noticed that the child was icteric and rather pale and had an enlarged spleen. There was no history of anæmia or jaundice in her own or her family's past record.

The results of serial blood examinations were summarized as follows. On admission, there were 2,700,000 red blood cells per cubic millimetre, of which 3·6% were reticulocytes; 62,000 leucocytes, of which 93% were neutrophile cells, 4% lymphocytes, 2% monocytes and 1% eosinophile cells; numerous thrombocytes; the hæmoglobin value was 7·0 grammes *per centum*, and the colour index was 0·86. On November 8, 1946, the total number of red blood cells per cubic millimetre had risen to 4,090,000, of which 6% were reticulocytes; the total leucocytes had dropped to 9,900 per cubic millimetre, of which 60% were neutrophile cells and 31% lymphocytes; the hæmoglobin value was 8·5 grammes *per centum* and the colour index 0·7. On November 22, 1946, the red blood cells totalled 2,660,000 per cubic millimetre, of which 7% were reticulocytes; a moderate degree of anisocytosis was present; the hæmoglobin value was 7·5 grammes *per centum* and the colour index was 0·96. On March 20, 1947, the total red blood cell count was 3,750,000 per cubic millimetre, being 4·8% reticulocytes; anisocytosis was still evident; the

hæmoglobin value was 9·5 grammes *per centum* and the colour index 0·85; the leucocytes numbered 16,200 per cubic millimetre. The results of examination for red cell fragility were as follows. On November 13, 1946, the hæmolysis began at a saline concentration of 0·72% and was complete at a concentration of 0·36%. On January 6, 1947, hæmolysis began at 0·64% and was complete at 0·04%. On March 21, 1947, hæmolysis began at 0·56% and was complete at 0·40%. Plain X-ray examination of the gall-bladder showed no abnormality. Urobilinogen was present in the urine when the patient was icteric.

For treatment the patient had been given ferrous sulphate by mouth. The progress in her general condition had been good except for the presence of dental sepsis. Icterus had been slight. The splenic enlargement had varied in degree, but it was usually about two and a half fingers' breadth below the costal margin. It was proposed to remove the spleen at a later date.

Cirrhosis following Infective Hepatitis.

Dr. Hughes's last patient was a girl who had been originally admitted to hospital on November 4, 1944, her age at that time being nine years. She had had jaundice for two months prior to her admission; the onset had been gradual and had not been preceded by any definite infectious process. There had been no complaint of pain or lethargy. The urine had been dark and the stools normal in colour. The jaundice had varied in its intensity. On examination at the time of admission the child was found to be jaundiced, and the liver and spleen were both palpable, two fingers' breadth and one finger's breadth respectively, below the costal margin. The Van den Burgh test gave a direct positive reaction. The urine contained bile pigments, salts and urobilinogen, but no tyrosine crystals. The results of a blood Wassermann test were negative. The red cell fragility was found to be within normal limits. The red blood cells numbered 4,240,000 per cubic millimetre, of which 0·5% were reticulocytes; the hæmoglobin value was 15·0 grammes *per centum* and the colour index 1·2.

Dr. Hughes explained that since the time of the child's original stay in hospital she had been attending the out-patient department. Her general health was good, her jaundice had persisted but varied in intensity, the splenic enlargement had also persisted and had increased slightly, and the liver had remained large until late in 1946, since when it had gradually decreased in size. Repeated blood counts had shown no evidence of hæmolysis. The fragility of the red blood cells had not increased. The hippuric acid excretion test was performed on July 21, 1945, the total excretion in four hours being 32% of normal. The provisional diagnosis was cirrhosis following infectious hepatitis.

Infantile Nutritional Œdema.

DR. KATHLEEN WINNING showed a female infant, aged eighteen months. This patient was an only child and had had an instrumental birth. She was breast fed until she was eight months old, after which time she had been given various milk mixtures, but did not appear to tolerate any of these and frequently vomited. For three to four weeks prior to admission to hospital she had been given orange juice and barley water only, these being the only substances that she did not vomit. The child was admitted to the Royal Alexandra Hospital for Children on January 30, 1947, the parents stating at the time that she had been "swollen" for two days. On examination generalized œdema of the face, trunk and extremities was found. The skin was waxy and pale. There were infected cracks at the corners of the mouth and also behind and below the ears. The fauces were slightly congested and there was no hæmorrhage in the skin nor in the gums. No abnormality was found in the chest, cardio-vascular system or central nervous system. There was no ascites. The child weighed seventeen pounds eight ounces. The urine was amber coloured, acid in reaction and without albumin; the centrifuged deposit contained about five cells per high-power field. The protein content of hæmolysed capillary blood was 4·2 grammes *per centum* (serum could not be obtained and its protein content was less than that of hæmolysed blood); the child thus had a hypoproteinæmia. A mild hypochromic anæmia was also found. The child was given the normal ward diet (about 900 Calories) and about 40 grammes of skim milk mixture (equal to 30 grammes of protein). Thus the daily protein intake was about 70 grammes, or seven grammes per kilogram. In addition the child was given 150 milligrammes daily of thiamin hydrochloride by intramuscular injection and 150 milligrammes daily of ascorbic acid. The fluid intake was not restricted. The œdema decreased immediately and had disappeared by the eighth day, the weight having fallen by over seventeen ounces. The child then began to gain weight. By the thirteenth day the protein content of the hæmolysed capillary blood had risen to 4·77 grammes *per centum*, and on the twenty-first day the weight was over seventeen and a half pounds, and the child was contented and taking food well. Dr. Winning commented that the œdema was due to the low serum proteins which had resulted from inadequate protein in the diet. There might also have been some thiamin deficiency.

Cœliac Disease.

DR. R. A. R. GREEN presented two patients suffering from cœliac disease. The first, a female child, aged twenty-one months, had been admitted to Goulburn District Hospital on December 4, 1946, with a provisional diagnosis of marasmus. It had been stated that lethargy, anorexia and loss of weight had been noted for three weeks before admission. Her weight at that time was fifteen pounds eight ounces. She had been receiving a full infant diet. In the first two weeks after admission her weight had risen to sixteen pounds four ounces; it had then fallen to sixteen pounds, and remained stationary for two weeks. It had then gradually fallen to fifteen pounds four ounces. Treatment given had included "Pentavite" three times a day, one tablet of ascorbic acid per day, iron and ammonium citrate emulsion twice a day, as well as an intramuscular injection of 0·25 millilitre of crude liver extract on every alternative day for three months. On February 25, 1947, the child had developed gastro-enteritis. It was stated that sulphaguanidine, of which one tablet was administered every four hours for one week, and penicillin (15,000 units three times a day *per rectum* for one week) were given. The result of a Mantoux test on February 28, 1947, was negative. On the same date X-ray examination of the chest revealed no abnormality, and the blood contained 4,500,000 red blood cells and 10,000 white blood cells per cubic millimetre; the hæmoglobin value was 65·0 grammes *per centum*. The child was transferred to the Royal Alexandra Hospital for Children on March 10, 1947, when she was found to be a thin, wasted infant, the wasting being particularly of the thighs and buttocks; the abdomen was protuberant and the fontanelle depressed. Her weight was fifteen pounds six ounces. No masses were palpable in the abdomen; examination of her lungs and throat revealed no abnormality. She was given normal ward diet. The treatment instituted consisted of three minims of "Adexolin", one drachm of "Vibex" and five minims of "Hepasol", all administered three times a day, and one millilitre of "Campolon" injected twice a week. A blood count on March 11, 1947, revealed 4,400,000 red blood cells and 7,700 white blood cells per cubic millimetre; the hæmoglobin value was 11·0 grammes *per centum*, the colour index 0·83 and the corpuscle index 88. On March 13, 1947, the child's weight had dropped to fourteen pounds fourteen ounces and she was refusing to take food. On March 22, 1947, the stool was analysed: macroscopically it was semi-solid and light yellow in colour; microscopic examination revealed occasional evidence of fatty material and quantities of cellulose residue, but no fat globules; chemical analysis showed that the total fat content of dried fæces was 36%, of which 92% was split and 8% unsplit fat. On March 26, 1947, a diet free from fat ("cœliac disease diet") was commenced. The child's condition then began to improve and she was soon eating well; her weight, however, did not show any improvement. X-ray examination of her chest had revealed no abnormality.

Dr. Green's second patient was a female child, aged three years, who had been quite well until December, 1945, when her mother noticed that the child was very thin, had a large abdomen, and was passing large, pale, offensive motions. She had been admitted to Grenfell Hospital where she was treated for six months for recurrent diarrhœa. The motions had been bulky, pale and frothy, and there was very little improvement during this period. She was admitted to the Royal Alexandra Hospital for Children on July 12, 1946, when her weight was eighteen pounds twelve ounces. She was described as a grossly wasted, apathetic child with marked frontal bossing of the skull. Her fontanelle had not closed. Her abdomen was distended, soft and doughy; no masses were palpable. Her teeth were poorly developed. No abnormality of her heart, lungs or throat was detected. Her blood contained 4,080,000 red blood cells per cubic millimetre, the hæmoglobin value was 11·0 grammes *per centum*, and the serum protein content was 5·12 milligrammes per 100 millilitres. The child was given a transfusion of 300 millilitres of blood on admission, and 120 millilitres of serum two days later. Treatment was commenced with three minims of "Adexolin" and one drachm of liquid "Vibex" three times a day, and one millilitre of "Campolon" administered intramuscularly twice a week. A diet free from fat was ordered. X-ray examination of the long bones on July 15, 1946, revealed an appearance suggestive of a nutritional disorder, but no evidence of rickets. A stool,

examined on June 17, 1946, was very pale and semi-solid; microscopic examination revealed the presence of cellulose residues and soap; the total fat content of dried fæces was 40%, of which 12% was split fat. By July 23, 1946, the total number of red blood cells had increased to 5,200,000 per cubic millimetre and the hæmoglobin value had risen to 14·5 grammes *per centum*. The child's weight had gradually increased, until it was twenty-one pounds seven ounces on September 9, 1946, when the child developed whooping-cough. Her weight on October 20, 1946, was twenty-two pounds twelve ounces, the abdomen was still distended, and marked wasting of the thighs and buttocks had persisted. The weight on November 10, 1946, was twenty-three pounds twelve ounces. From November, 1946, until January, 1947, the weight had steadily dropped, the lowest finding being eighteen pounds fifteen ounces. A blood count in December, 1946, revealed 4,600,000 red blood cells per cubic millimetre; the hæmoglobin value was 14·0 grammes *per centum*. From January to April, 1947, the weight had varied between eighteen pounds and twenty-one pounds. The protein content of the diet was increased to fifteen grammes per kilogram in February, 1947. X-ray examination of her chest in March, 1947, revealed no abnormality.

Anæmia Possibly of Hæmolytic Origin.

Dr. Green's last patient was a male infant, aged twelve months, who had been admitted to hospital on January 26, 1946. The infant had been born by a normal delivery at full term, his birth weight being six pounds fifteen ounces. It was stated that prior to admission he had always been pale; he had had a gastro-intestinal upset lasting for five days, but had otherwise been well; he had never been jaundiced. On examination the infant was found to be extremely pale. The spleen was palpable, but the liver was not palpable. Clinical examination of the lymph glands and of the other systems revealed no abnormality. A transfusion of four ounces of blood was administered, and the child was discharged from hospital on July 12, 1946. On July 23, 1946, he was readmitted and received a further transfusion of four ounces of Rh-negative blood. The response to the Van den Bergh test at that time was negative. Estimation of the red blood cell fragility on August 3, 1946, revealed that hæmolysis commenced at a saline concentration of 0·44% and was complete at 0·32%. A further four ounces of Rh-negative blood was administered on August 7, 1946. X-ray examination of the long bones, chest and skull was made on October 21, 1946; the report on the appearances of the long bones was as follows: "The cortex of the bones of the upper extremities appears to be usually thin and the trabeculation somewhat lesser in character, suggesting some over-activity of the bone marrow; otherwise no changes can be seen." No abnormalities were seen in the chest and skull. A test for red blood cell fragility on October 24, 1946, revealed that hæmolysis commenced at a saline concentration of 0·56% and was complete at 0·32%—an increase in fragility. No blood was detected in the stools or urine at this time. Further transfusions, each of four ounces of blood, were given on November 19 and 28, 1946. The liver and spleen were palpable at that time. The red blood cells still showed increased fragility in January, 1947. In February, 1947, the child was admitted to hospital, the intention being to perform splenectomy; but as the blood count showed improvement he was discharged without operation. A further transfusion had been given during April.

Cretinism.

DR. S. G. BRADFIELD showed a female patient, aged seven months. Her mother had been quite well during pregnancy and had had a normal confinement. The infant had seemed well until three months of age. She had been breast fed till she was two months old and had then been given modified cow's milk. On January 16, 1947, the child had been brought to the out-patient department of the Royal Alexandra Hospital for Children, her age then being four months. It was stated that she was a slow feeder, taking about two ounces of modified milk in forty-five minutes; she had been constipated and pale with limpness of muscles and "snuffling" in the nose. On examination the skin was dry, the complexion pale, and the forehead was very wrinkled; her movements were slow, she had a husky cry, the tongue was enlarged and protruding, the abdomen was protuberant, and an umbilical hernia was present. The pulse rate was 108 per minute. Her weight (clothed) was fifteen pounds eight ounces. The thyreoid gland was not palpable. Administration of *Thyreoideum Siccum* was commenced, one-quarter of a grain being given twice a day. The blood count on February 3, 1947, revealed 2,230,000 red blood cells and 12,500 white blood cells per cubic millimetre; the hæmoglobin value was 8·0 grammes *per centum* and the colour index was 1·2. At the time of the clinical meeting the child seemed well. Her pulse rate was 140 per minute, her weight was eighteen pounds two ounces. She took her feeds in fifteen minutes, and she played with a rattle, but did not pull herself up to a sitting position. Her lower incisor teeth were erupting, she still had a protruding tongue and some wrinkling of the forehead, the muscles of the neck and back were weak, and the skin was smooth and moist. Dr. Bradfield considered that the infant was a typical cretin of the sporadic type, the symptoms having appeared at the usual age (three months); the response to treatment had been satisfactory.

Achondroplasia and Hydrocephalus.

Dr. Bradfield's second patient was a female child, aged eleven months, who had been born at the Women's Hospital, Crown Street, Sydney, on May 1, 1946, with a birth weight of six pounds four ounces. There had been a brow presentation and an instrumental delivery after labour lasting for eight and a half hours. The condition of the infant had not been satisfactory during the first two or three weeks after birth. She had collapse of the left lung and anæmia and was given a course of sulphadiazine and of penicillin followed by iron. During infancy her weight gain had been slow, she was backward in sitting up, the skull was always large with widely open anterior fontanelle, and muscular hypotonia was noticed. The anæmia had decreased. X-ray examination of the skull in October, 1946, revealed that the head was enlarged, with a shallow bilocular pituitary fossa suggestive of hydrocephalus. At that time the child was admitted to the Royal Alexandra Hospital for Children under the care of Dr. T. Y. Nelson. Examination by encephalogram showed mild dilatation of the right lateral ventricle and fluid-filled spaces in the cortex suggesting cerebral agenesis. X-ray examination of the lung bones showed the appearances of achondroplasia. The cerebro-spinal fluid was normal. Dr. Nelson had considered that the hydrocephalus was partly compensatory and partly associated with shortening of the base of the skull and kinking of the aqueduct due to achondroplasia. At the time of the meeting the infant could not pull herself up to a sitting position, but could stand on her head. Intelligence appeared normal. She weighed fourteen pounds. The skull showed marked prominence of the frontal region with a widely open anterior fontanelle; its circumference was nineteen and a half inches. The face was small compared to the size of the skull; the bridge of the nose was depressed; dental development was normal. The trunk appeared normal in length; the limbs were short, especially the upper arms and thighs; the spine was poorly supported and flexed excessively at the lumbar region when the infant was held in a sitting position; the abdomen was protuberant; and "trident hand" was present. Investigation of the family history revealed no definite cases of achondroplasia. The sister of the child's father had a prominent forehead and short limbs, her height being four feet ten inches. Dr. Bradfield considered that the infant showed the typical appearances of achondroplasia combined with a mild degree of hydrocephalus.

Bronchiectasis.

DR. N. H. MEACLE showed a series of X-ray photographs of children suffering from bronchiectasis. The first child, a female patient, aged seven and a half years, had had cough with sputum and periodical attacks of pneumonitis since infancy. On examination slight deformity of the chest and emphysema on the right side were found. Clubbing of the fingers was present. A bronchogram revealed extensive saccular bronchiectasis with ecterectosis of the lower lobe of the left lung. For treatment this lobe had been removed.

The next patient was a girl, aged nine years, who had had cough with sputum following pneumonia at the age of fifteen months. She was a thin child, poorly nourished. Examination of her lungs revealed flattening of both bases with poor air entry and crepitations at the left base. A bronchogram revealed left basal bronchiectasis of the cylindrical type. For treatment it was proposed to perform lobectomy after a period in hospital during which bronchoscopic suction would be performed and "aerosol" penicillin would be administered.

The third child, also a girl, aged nine years, had had cough with sputum since infancy and had suffered from measles and pertussis at the age of five years. Examination of her chest revealed dulness and almost absent air entry throughout the extent of the left lung. The mediastinum was displaced to the left. An old abscess of the left lung with gross bronchiectasis of the whole lung was revealed by bronchogram. A left pneumonectomy had been performed. Examination of the lung after removal showed generalized bronchiectasis with the presence of an abscess cavity.

The fourth patient, a boy, aged five years, had had a chronic cough with sputum following pneumonia and pink disease at the age of six months. Examination revealed a poor nutritional state; and there were diminished expansion

at the base of both lungs, bronchial breathing and râles at the base of the right lung, and a few crepitations at the base of the left lung. A bronchogram showed saccular bronchiectasis at the base of the right lung; the left base was involved to a lesser extent. The treatment recommended was the administration of sulphathiazole for an indefinite period.

The next patient, a girl, aged twelve years, had had a chronic cough since the age of two years following measles and whooping-cough. Her nutrition was poor and she had a moist cough with a moderate amount of sputum. Examination of her lungs revealed diminished air entry at both bases and in the region of the left axilla. Bronchography showed bilateral basal saccular bronchiectasis. The treatment recommended was repeated bronchoscopic suction.

The sixth patient, a boy, aged nine years, had had measles and bronchopneumonia at the age of eighteen months. He had had cough with sputum (up to one ounce daily) ever since; the sputum was offensive. On examination his nutrition was found to be poor, and there was diminished expansion of the chest in the region of the lower lobe of the left lung with diminished breath sounds. The fingers were slightly cyanotic and showed early clubbing. A bronchogram revealed small areas of saccular bronchiectasis at the anterior costo-phrenic angle on the left side. Mild cylindrical dilatation of the posterior basal bronchi was seen on the left side. Conservative treatment for a period of six months was considered advisable with review at the end of that time.

The next child discussed was a girl, aged six years, who had had cough with plentiful offensive sputum since she had suffered from pink disease at the age of six months. On examination her nutrition was good; her fingers were clubbed and cyanotic. Examination of her chest revealed numerous râles at the bases of both lungs and decreased air entry at the left base. A bronchogram revealed bilateral saccular basal bronchiectasis with areas of emphysema and collapse of the right lower lobe. It was proposed to perform a bilateral lower lobe lobectomy in stages.

The last patient discussed by Dr. Meacle was a boy, aged three years, who had had a cough since he had had pink disease at the age of eighteen months. He had also had measles. During the six months prior to the meeting he had had four attacks of bilateral consolidation at the bases of the lungs. His tonsils and adenoids had been removed. On examination it was found that nutrition was poor and the child was pale. Examination of the left lower part of the chest revealed diminished movement and decreased breath sounds with moist accompaniments; a few crepitations were detected at the base of the right lung. A bronchogram showed advanced saccular bronchiectasis in the left lower lobe and possible early bronchiectasis at the right base. After the child had been treated in hospital for one month with "aerosol" penicillin, weekly bronchoscopic lavages and breathing exercises, the signs had become less to the left base. At the time of the meeting patient was receiving sulphathiazole daily and his condition would be reviewed after six months with a view to lobectomy.

Talipes Equino-Varus.

DR. W. L. MACDONALD presented identical twins, two female infants, aged eight weeks, both suffering from right *talipes equino-varus*. All the usual elements of the deformity were present; they were being treated by daily manipulations and strapping.

Dr. MacDonald's next patient was a boy, aged three months, who had attended the out-patient department at the age of one month with congenital *talipes equino-varus* of the right and left feet. The deformity was mild in the right foot, but was more severe in the left foot. The child had been treated with daily manipulations and strapping and later with Dennis Brown's splints. Dr. MacDonald considered that the patient would respond well to treatment.

Congenital Syphilis.

Dr. MacDonald's last patient was a male infant, aged thirteen weeks. The infant had been well until February 28, 1947, when it was noticed that he did not use his left arm. On examination resistance to most movements of the joints of the arm was apparent, and tissue-paper scars were noticed on the left arm. X-ray examination revealed erosion of the left acromion, of both sides of the left olecranon, of both tibiæ and of the medial ends of both femora. These lesions were considered typical of congenital syphilis. The Wassermann test gave a positive result. Anti-syphilitic treatment was commenced, 0·02 millilitre of bis-glucol being injected weekly. Improvement had been noted after the first injection.

Congenital Cyst of Tibia.

DR. R. L. STEPHEN presented a male patient who had been first admitted to hospital in April, 1945, his age then being four months; the history was that he had been born with a twisted left leg which had become painful and had been held immobile for one week. On examination the left lower limb was found to be flaccid, although there was active movement in the foot. X-ray examination showed fibrocystic disease of the left tibia and fibula with doubtful evidence of a fracture superimposed. The leg was put in a plaster of Paris cast and the baby discharged to the out-patient department. The next admission to hospital was eight months later when the left leg was found, on removal of the plaster at the out-patient department, to be grossly swollen with marked deformity of the tibia. A plaster of Paris hip spica was applied and the patient discharged again to the out-patient department. Three months later the infant was again admitted to hospital, his age then being fifteen months, with a grossly swollen left thigh and leg. X-ray examination showed a fresh fracture below the original lesion. A plaster of Paris cast was applied to the left thigh and leg, and the patient again became an out-patient. X-ray examination ten months later, on January 13, 1947, provided evidence that very little union had occurred. The child was admitted to hospital one month later with a false joint in the lower third of the left tibia and a gross out-bowing deformity with one and a half inches of shortening. A plaster of Paris cast was applied, extension being made on the limb during application of the cast. The child was discharged. Just under one month later he was readmitted, the plaster was removed and the leg was exercised in bed for one week. X-ray examination on March 13, 1947, showed no definite evidence of bony union. Operation was undertaken at which the cyst wall was excised, the bone ends were freshened and the periosteum was oversewn. A plaster of Paris hip spica was applied. A section of the cyst was reported on by the pathologist as follows:

> Microscopically—a narrow, dense collagenous zone which merges with an irregular layer of spindle celled fibrous tissue, similar to that which occurs in repair of bones. No new formed trabeculæ of bone are present, however.

The provisional diagnosis was congenital bone cyst.

(To be continued.)

NEW SOUTH WALES BRANCH NEWS.

THE following books, pamphlets *et cetera* have been added to the library of the New South Wales Branch during the period February 1, 1947, to June 30, 1947.

Abt, Isaac A.: "1946 Year Book of Pediatrics."
Association for Research in Nervous and Mental Disease: "Military Neuropsychiatry", 1946.
Commonwealth of Australia.—Industrial Welfare Division Booklets: No. 1—"How to Reduce Absenteeism and Increase Production", 1943. No. 3—"Industrial Accident Records", 1945. Industrial Welfare Division Bulletin: No. 9—"Selection and Placement of New Employees", 1946.
Bethea, O. W.: "1946 Year Book of General Therapeutics."
Blaine, Anite, *et alii*: "The World at the Crossroads", 1946.
Bothman, Louis, *et alii*: "1946 Year Book of Eye, Ear, Nose and Throat."
British Oxygen Company, Limited.: "Oxygen in War and Peace", 1946.
Burnet, F. M.: "Background of Infectious Diseases in Man", 1946.
Christopher, Frederick: "Textbook of Surgery", Fourth Edition, 1946.
Coppleson, V. M.: "Clinical Handbook", Third Edition, 1946.
Cox, L. B., and Tolhurst, J. C.: "Human Torulosis", 1946.
Curran, D., and Guttmann, E.: "Psychological Medicine", Second Edition, 1945.
Cushny, A. R.: "Pharmacology and Therapeutics", Thirteenth Edition, revised by A. Grollman and D. Slaughter, 1947.
Davis, Loyal: "Principles of Neurological Surgery", Third Edition, 1946.
Dick, G. F., *et alii*: "1946 Year Book of General Medicine."
Dyke, S. C.: "Recent Advances in Clinical Pathology", 1947.
Fairbrother, R. W.: "Textbook of Bacteriology", Fifth Edition, 1946.
Goldmann, Franz: "Public Medical Care", 1945.
Graham, E. A.: "1946 Year Book of General Surgery."
Great Britain.—Medical Research Council, Special Reports: No. 255—"Chemotherapeutic and Other Studies of Typhus", by Van den Ende *et alii*, 1946. No. 258—"Preservation of Proteins by Drying", by R. I. N. Greaves, 1946.
Greenhill, J. P.: "1946 Year Book of Obstetrics and Gynecology."

XUM

Haggard, H. W.: "Devils, Drugs and Doctors", 1929.
Hastings, Donald W., *et alii*: "Psychiatric Experiences of the Eighth Air Force: First Year of Combat, 1942-43."
Holmes, Gordon: "Introduction to Clinical Neurology", 1946.
Joslin, E. P.: "Treatment of Diabetes Mellitus", Eighth Edition, 1946.
Kovács, R.: "1946 Year Book of Physical Medicine."
Lee, Douglas H. K.: "Physiology of Tissues and Organs", 1946.
Lewis, Thomas: "Vascular Disorders of the Limbs", Second Edition, 1946.
Lowsley, O. S.: "1946 Year Book of Urology."
Luck, J. M.: "1947 Annual Review of Physiology."
MacKee, G. M., and Cipollaro, A. C.: "X-rays and Radium in the Treatment of Diseases of the Skin", Fourth Edition, 1946.
McQuarrie, Irvine: "Brennemann's Practice of Pediatrics", four volumes, 1947.
National Foundation for Infantile Paralysis: "Bibliography of Infantile Paralysis, 1789-1944", 1946.
Nelson, Waldo E.: "Mitchell-Nelson Textbook of Pediatrics", Fourth Edition, 1946.
Novak, Emil: "Gynecological and Obstetrical Pathology", Second Edition, 1947.
O'Brien, Marjorie: "Workers' Compensation Law in N.S.W., 1926-1946", Second Edition.
Painter, C. F.: "1946 Year Book of Industrial and Orthopedic Surgery."
Paterson, Donald: "Sick Children", Sixth Edition, 1947.
Ranson, S. W.: "Anatomy of the Nervous System", Eighth Edition, 1947.
Robb, Douglas: "Health Reform in New Zealand", 1947.
Rogers, Leonard, and Muir, Ernest: "Leprosy", Third Edition, 1946.
Russell, P. F., *et alii*: "Practical Malariology", 1946.
Sadler, William S.: "Modern Psychiatry", 1945.
Schwedel, John B.: "Clinical Roentgenology of the Heart", 1946.
Stokes, E. H.: "Cardio-vascular and Respiratory Sounds", 1946.
Sulzberger, M. B., and Baer, R. L.: "1946 Year Book of Dermatology and Syphilology."
University of Sydney: "Senior Year Book, 1946-47, of Faculty of Medicine."
Urbach, Erich: "Skin Diseases, Nutrition and Metabolism", 1946.
Wesson, Miley B.: "Urologic Roentgenology", Second Edition, 1946.
Wintrobe, M. M.: "Clinical Hematology", Second Edition, 1946.
Worrall, R. L.: "The Outlook of Science", Second Edition, 1946.

Journals.—Abstracts of World Medicine, Volume I, 1947; *Abstracts of World Surgery, Obstetrics and Gynæcology*, Volume I, 1947; *American Practitioner*, 1947; *Anæsthesia*, Volume I, 1946; *Anesthesia Abstracts*, No. 21, 1946; *Australasian Journal of Pharmacy*, Volume XXVIII, 1947; *British Journal of Social Medicine*, Volume I, 1947; *Chemical Abstracts*, Volume XLI, 1946; *New Modern Drugs*, 1946; *Poliomyelitis Current Literature*, Volume I, 1946; *Plastic and Reconstructive Surgery*, Volume I, 1946; *Southern Medical Journal*, 1947.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Numbers 111, 116 and 121, of June 26, July 3 and 10, 1947.

AUSTRALIAN MILITARY FORCES.

Australian Army Medical Corps.

VX39490 Captain H. B. Hattam is placed upon the Regimental Supernumerary List (leave without pay), 16th January, 1946, to 1st January, 1947, and is again placed upon the Regimental Supernumerary List, 2nd January, 1947.

VX12974 Lieutenant-Colonel (Temporary Colonel) J. M. Blair, O.B.E., relinquishes the rank of Temporary Colonel and is transferred to the Reserve of Officers (Australian Army Medical Corps) with the rank of Lieutenant-Colonel and is granted the honorary rank of Colonel, 20th February, 1947.

Reserve Citizen Military Forces.

Australian Army Medical Corps.

2nd Military District.—Honorary Captain I. C. Morrison is retired, 24th February, 1947.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

The appointments of the following officers are terminated on demobilization: Temporary Squadron Leader (Acting Wing Commander) G. G. Burniston (261263), 13th May, 1947; Flight Lieutenants F. P. Champion de Crespigny (255171), 5th May, 1947, and J. R. Tripp (267568), 7th May, 1947.

The appointment of Flight Lieutenant R. E. Buckingham (267680) (part time) is terminated, 1st May, 1947.

The appointment of Flight Lieutenant J. H. S. Waters (267226) is terminated on demobilization, 15th May, 1947.

Reserve: Medical Branch.

The following ex-officers are appointed to commissions with the temporary ranks as shown: Squadron Leader John Stephen Boxall (263226), 12th May, 1947; George Garrett Burniston (261263), 14th May, 1947; Flight Lieutenant Reginald Eric Buckingham (267680), 2nd May, 1947; Jeffery Robert Tripp (267568), 8th May, 1947.

James Howard Stewart Waters (267226) is appointed to a commission with the rank of Flight Lieutenant, 16th May, 1947.

Post-Graduate Work.

THE UNIVERSITY OF QUEENSLAND POST-GRADUATE MEDICAL EDUCATION COMMITTEE.

THE University of Queensland Post-Graduate Medical Education Committee announces that it is proposed, if sufficient persons are interested, to commence post-graduate instruction in anatomy and physiology suitable for medical graduates who are preparing for higher qualifications in medicine or surgery, or who wish merely to revise these subjects. Classes will be held weekly in each subject on evenings to be arranged. Anatomy will include embryology and histology, also dissection. Classes will commence as soon as sufficient applications are received.

Full particulars, including fees, are available to any person desiring them on application to the Director of Post-Graduate Studies, British Medical Association House, 225, Wickham Terrace, Brisbane.

Obituary.

LEONARD HARWICK FOOTE.

DR. LEONARD HARDWICK FOOTE, whose death was recently recorded, was born at Ipswich, Queensland, in 1894 and was educated at the Ipswich Grammar School, winning a university scholarship in 1912.

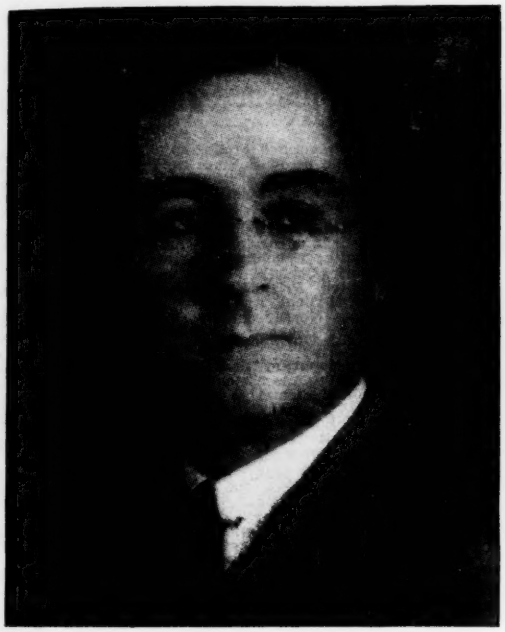
He completed his first year of engineering at the University of Queensland while resident at King's College, representing his university in cricket and football, and the State in football. On the outbreak of war in 1914 he enlisted in the Australian Army Medical Corps, and went through the Gallipoli campaign as a stretcher-bearer in the Third Field Ambulance, celebrating his twenty-first birthday on the Peninsula.

After the transfer of the Australian Imperial Force to France he was transferred to an officers' school at Cambridge, and after graduation was posted to the Ninth Infantry Battalion. His period as a combatant officer was, however, very brief, as he sustained a severe chest wound shortly after joining this unit. After a long convalescence he was returned to Australia medically unfit.

In 1918 he resumed his university career, transferring his affections to medicine at the University of Sydney. He was one of the inaugural students of Wesley College, Sydney, and represented the college in tennis, cricket and rifle shooting. He graduated M.B., Ch.M. in 1922, and after a period as resident medical officer, first at the Royal Prince Alfred Hospital and then at the Brisbane Hospital, commenced practice at Greenslopes in 1923, and later moved to Vulture Street, South Brisbane.

In 1923 he married Ida, only daughter of Professor and Mrs. Scott Fletcher, at that time Master of Wesley College. On the outbreak of war in 1939 he became D.A.D.M.S., Northern Command, and later A.D.M.S., which position he held until forced to retire by illness in 1943. On his return to civil life he was forced to give up the arduous life of a general practitioner, and specialized in anæsthetics, becoming anæsthetist to the 112 Brisbane Military Hospital and honorary anæsthetist at the Mater Misericordiæ Public Hospital, Brisbane. He has been described as a "natural" anæsthetist; his common sense and placid nature always gave patient and surgeon the greatest confidence. In December, 1946, however, he sustained a further coronary catastrophe to which, after a long and courageous struggle, he finally succumbed on June 5, 1947. He is survived by his widow and four children, two of whom are at present third year medical students at the University of Queensland.

Dr. K. B. Fraser writes: I first remember Len Foote as a strong-running centre threequarter in the University of Queensland and State Rugby Union football teams in 1913.



He enlisted on the outbreak of war in 1914, and served first as a stretcher-bearer in a field ambulance on Gallipoli and later as a subaltern in the famous Ninth Battalion in France.

Seriously wounded in the chest, he returned to Australia after a long convalescence, and commenced his medical course at Wesley College, University of Sydney, in 1918. He quickly became senior student at Wesley, where he exercised a wonderful influence on the college during its early years.

In those days he played both cricket and football for Wesley with the wound in his chest carefully padded up with cotton wool. He also played a few games with the University of Sydney First XI, his favourite shot being the cover drive, which he executed with great power and skill.

Returning to Queensland after his marriage, he built up a large practice in South Brisbane, and became a part-time physician at the Brisbane General Hospital.

Immediately on the outbreak of war in 1939 he enlisted again. Unfit for field service, he was appointed D.A.D.M.S., Queensland Lines of Communication Area, a post he was particularly well qualified to fill in virtue of his administrative ability, his sound judgement and the universal respect in which he was held by all members of the profession. He subsequently became A.D.M.S., and filled this position until he was discharged medically unfit in March, 1944.

From December, 1942, until March, 1944, it was my privilege to work in very close association with him. During those years I learnt something of the solid worth of Len Foote; his memory, his energy and his attention to detail were prodigious; forthright to a degree, he was intolerant of anything savouring of selfishness or self-interest, but never spared himself in his efforts to help medical officers who were in difficulties, and many medical units owed their smooth transit through the area to his unflagging efforts.

There is no doubt that his grievous wound in the First World War, and the strain imposed upon him during the years 1939-1944, materially hastened his end.

The last time I saw him, a few days before he died, he talked of rugby football, the game which he loved, with no mention at all of his own protracted and distressing illness.

A man of great courage and high ideals, Leonard Hardwick Foote lived a life of service to his country, his patients and his family, and passes from our midst leaving behind him an abiding memory of unselfishness and devotion to duty.

The Royal Australasian College of Physicians.

MEETINGS OF THE COLLEGE.

THE ordinary meeting of the Royal Australasian College of Physicians in 1947 will be held in Sydney on Thursday and Friday, October 23 and 24, 1947.

The annual meeting in 1948 will be held in Brisbane on Thursday and Friday, June 10 and 11, 1948.

EXAMINATIONS FOR MEMBERSHIP.

AN examination for membership of the Royal Australasian College of Physicians will take place in September-October, 1947. The written examination will be held in capital cities of the Commonwealth where candidates are offering. The clinical examination will take place in Sydney. Only those candidates whose answers in the written examination have attained a standard satisfactory to the Board of Censors will be allowed to proceed to the clinical examination.

The written examination will be conducted in capital cities on Saturday, September 20, 1947. The clinical examination will be conducted in Sydney on Tuesday, Wednesday and Thursday, October 20, 21 and 22, 1947.

Applications to appear before the Board of Censors should be made in the prescribed form and must be in the hands of the Honorary Secretary of the College not later than Saturday, August 23, 1947. Application forms are obtainable from the Honorary Secretary, 145, Macquarie Street, Sydney.

An examination for membership will also be held in May-June, 1948. The clinical examination will be conducted in Sydney early in the month of June. If a sufficient number of candidates is offering a clinical examination will also be conducted in Brisbane, the tentative dates for this examination being June 8 and 9, 1948.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Adamson, John Richmond, M.B., B.S., 1943 (Univ. Sydney), 8, Duntroon Avenue, Roseville.

Somerville, Don McLachlan, M.B., B.S., 1946 (Univ. Sydney), Base Hospital, Orange, New South Wales.

Seymour, John Henry, M.B., B.S., 1946 (Univ. Sydney), 68, High Street, North Sydney.

Jagers, Leslie James, M.B., 1944 (Univ. Sydney), Oaks Avenue, Dee Why.

Rumore, Anthony, provisional registration, 1947 (Univ. Sydney), Sydney Hospital, Macquarie Street, Sydney.

Walker, Reginald Gordon, provisional registration, 1947 (Univ. Sydney), 23, Stratford Avenue, Denistone, via West Ryde.

Frank, Alexander, registered in accordance with the provisions of Section 17 (*b*) of the *Medical Practitioners Act*, 1938-1945, 235, Macquarie Street, Sydney.

Coen, Kevin, M.B., B.S., 1936 (Univ. Sydney), 215, Macquarie Street, Sydney.

Doherty, John William, M.B., B.S., 1946 (Univ. Sydney), 46, Anglo Road, Campsie.

Fitzhardinge, Arthur Noel Berkeley, M.B., B.S., 1940 (Univ. Sydney), 19, Fairfax Road, Bellevue Hill.

Gray, Eva, provisional registration, 1947 (Univ. Sydney), 44, Bellevue Road, Bellevue Hill.

Greenberg, Harris Neville, provisional registration, 1947 (Univ. Sydney), 241, Birrell Street, Bondi.

Grieve, David Amor Harvey, provisional registration, 1947 (Univ. Sydney), Western Suburbs Hospital, Croydon.

Huth, Emil, M.B., B.S., 1946 (Univ. Sydney), 679, New South Head Road, Rose Bay.

Landecker, Hans Martin, registered in accordance with the provisions of Section 17 (*b*) of the *Medical Practitioners Act*, 1938-1945, 525, New South Head Road, Double Bay.

Lucas, Otto Nathan, registered in accordance with the provisions of Section 17 (*b*) of the *Medical Practitioners Act*, 1938-1945, 201, Macquarie Street, Sydney.

Morris, Walter John, M.B., B.S., 1945 (Univ. Sydney), 6, Brierley Street, Cremorne.

Newman, Neville Maurice, M.B., B.S., 1946 (Univ. Sydney), 29, Beresford Road, Rose Bay.

Nicholson, Elinor Catherine, M.B., B.S., 1946 (Univ. Sydney), The Hermitage, Blaxland Road, Ryde.

Brown, Douglas Scott, provisional registration, 1947 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Hammond, Henry Grant, M.B., B.S., 1944 (Univ. Adelaide), c.o. Brady's Hotel, South Broken Hill.

Deithe, Lyle George, provisional registration, 1947 (Univ. Sydney), 5, Pembroke Flats, 15, New South Head Road, Vaucluse.

Notice.

THE Secretary of the New South Wales Medical Defence Union, Limited, wishes to remind members that July 31, 1947, is the last day for the receipt of nominations for the position of councillor of the Union.

Medical Appointments.

Dr. A. G. Childs has been appointed a member of the advisory committee on technical courses at Guyra, New South Wales.

Dr. R. G. Williams has been appointed an examiner, in pursuance of the provisions of *The Nurses Registration Act*, 1921-1946, of Western Australia.

The following appointments as honorary clinical assistants have been made to the Royal Adelaide Hospital, Adelaide: Medical Section, Dr. R. N. C. Bickford, Dr. H. J. Edelman, Dr. M. W. Miller, Dr. J. M. McPhie, Dr. R. A. A. Pellew, Dr. C. T. Piper, Dr. J. W. Sangster and Dr. R. F. West. Surgical Section, Dr. W. E. B. Boscence, Dr. A. G. Campbell, Dr. D. C. Dawkins, Dr. G. M. Hone, Dr. B. G. Johnston, Dr. T. D. Kelly, Dr. L. J. T. Pellew, Dr. J. L. S. Scott, Dr. M. Y. Sheppard, Dr. G. H. Solomon, Dr. G. McL. Turnbull and Dr. G. W. Verco. Allergy Clinic, Dr. J. E. Bateman. Ophthalmological Section, Dr. D. O. Crompton, Dr. T. L. McLarty, Dr. S. Pearlman and Dr. A. W. Thrush. Dermatological Section, Dr. W. Gilfillan, Dr. A. J. Hakendorf, Dr. C. H. Schafer and Dr. F. G. T. Turner. Radiotherapy Section, Dr. R. de G. Burnard and Dr. B. C. Smeaton. Radiological Section, Dr. R. de G. Burnard, Dr. J. B. Thiersch and Dr. P. W. Verco. Gynæcological Section, Dr. A. D. Byrne, Dr. H. E. Pellew and Dr. R. L. Verco. Sterility Clinic (Male Section), Dr. R. A. Isenstein. Sterility Clinic (Female Section), Dr. H. E. Pellew. Orthopædic Department, Dr. N. P. Wilson.

Books Received.

"Dynamic Aspects of Biochemistry", by Ernest Baldwin, B.A., Ph.D.; 1947. Cambridge: The University Press. 8½" × 5½", pp. 470. Price: 21s.

"The Birth of a Child: Obstetric Procedure in Normal Childbirth for Those Who Attend Women in Labour", by Grantly Dick Read, M.A., M.D.; 1947. London: William Heinemann (Medical Books), Limited. 7¾" × 4¾", pp. 108. Price: 5s.

"Handbook of Elementary Anatomy: Specially Prepared for First Aid Students, Student Nurses, et Cetera", by John J. Teklenburg; 1947. London: H. K. Lewis and Company, Limited. 9¼" × 6", pp. 36, with 16 coloured illustrations. Price: 5s. 6d.

"Blind Intubation and the Signs of Anæsthesia", by J. U. Human, M.R.C.S., L.R.C.P., L.D.S., D.A.; Third Edition; 1947. London: H. K. Lewis and Company, Limited. 6¾" × 4", pp. 240, with illustrations. Price: 10s.

"A Textbook on the Nursing and Diseases of Sick Children for Nurses", by various authors, edited by Alan Moncrieff, M.D., F.R.C.P.; Fourth Edition; 1947. London: H. K. Lewis and Company, Limited. 8½" × 5½", pp. 758, with many illustrations. Price: 30s.

Diary for the Month.

JULY 31.—New South Wales Branch, B.M.A.: Branch Meeting.
AUG. 1.—Queensland Branch, B.M.A.: Branch Meeting.
AUG. 5.—New South Wales Branch, B.M.A.: Organization and Science Committee.
AUG. 6.—Western Australian Branch, B.M.A.: Council Meeting.
AUG. 6.—Victorian Branch, B.M.A.: Branch Meeting.
AUG. 7.—South Australian Branch, B.M.A.: Council Meeting.
AUG. 8.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute; Brisbane City Council (Medical Officer of Health). Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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